

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

John Alexander Edgar

Title:

ANTI CANCER AGENT AND

METHOD OF TREATMENT OF

CANCER

Appl. No.:

10/088,078

Filing Date:

07/22/2002

Examiner:

Unassigned

Art Unit:

Unassigned

CLAIM FOR CONVENTION PRIORITY

Commissioner for Patents Washington, D.C. 20231

Sir:

The benefit of the filing date of the following prior foreign application filed in the following foreign country is hereby requested, and the right of priority provided in 35 U.S.C. § 119 is hereby claimed.

In support of this claim, filed herewith is a certified copy of said original foreign application:

AUSTRALIAN Patent Application No. PQ 3148 filed 09/29/1999.

Respectfully submitted,

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Date July 22, 2002

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Patent Office Canberra

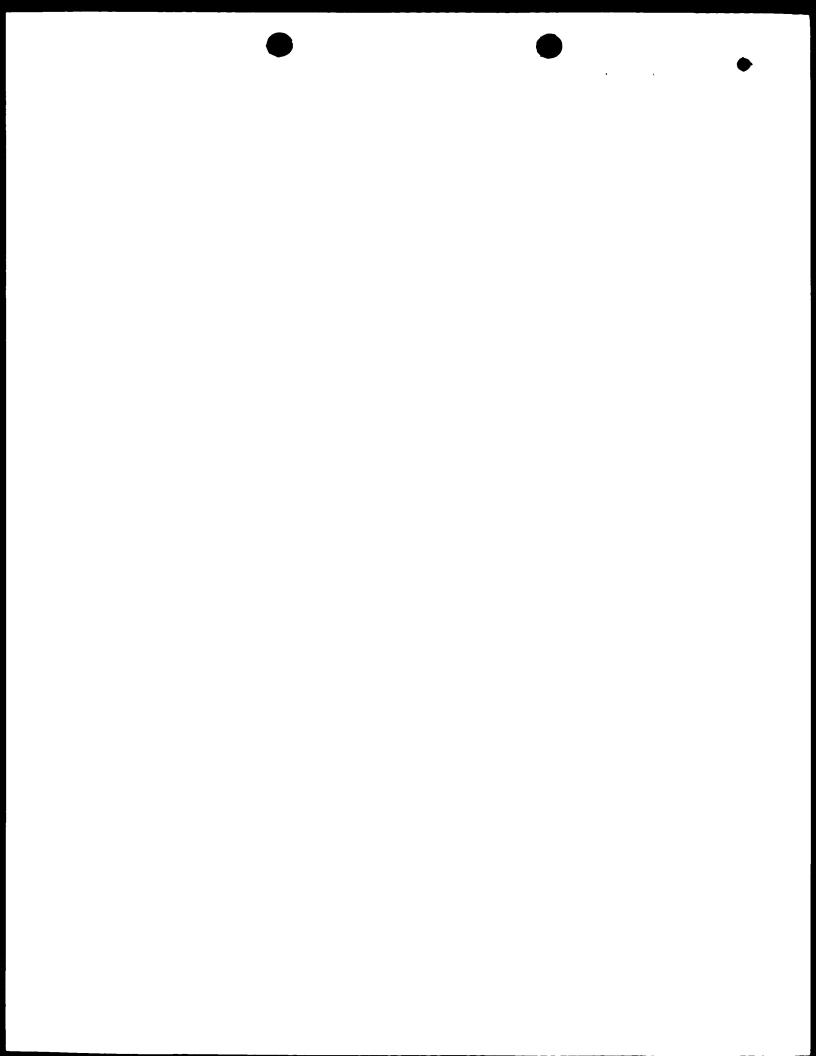
I, LEANNE MYNOTT, MANAGER EXAMINATION SUPPORT AND SALES hereby certify that annexed is a true copy of the Provisional specification in connection with Application No. PQ 3148 for a patent by COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION filed on 29 September 1999.

> WITNESS my hand this Twenty-second day of May 2002

LEANNE MYNOTT

MANAGER EXAMINATION SUPPORT

AND SALES



AUSTRALIA Patents Act 1990

PROVISIONAL SPECIFICATION

Invention Title:ANTI CANCER AGENT AND METHOD OF TREATMENT OF CANCER

Applicant: COMMONWEALTH SCIENTIFIC & INDUSTRIAL RESEARCH ORGANISATION

The invention is described in the following statement:

ANTI CANCER AGENT AND METHOD OF TREATMENT OF CANCER

The present invention relates to the treatment of cancer and to compositions for use in treatment of cancer.

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The search for anti-cancer agents has been, and remains, a major endeavour of the pharmaceutical industry, academic institutions and government agencies throughout the world. One of the significant problems with many cancer treatments is the severe adverse affects they have on the patient and non-cancerous tissues.

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We have now found that phomopsin mycotoxins (hereafter referred to as phomopins) and their derivatives exhibit potent anticancer activity. We have also found that phomopsins exhibit selective activity against liver cancer. Without wishing to be bound by theory we believe that phomopsins exhibit selectivity for liver cancers due to a tendency of phomopsin to accumulate in the liver. It will be appreciated that the selectivity of phomopsin in treatment of liver cancer is a significant advantage as it allows liver cancers to be targeted while minimising the effects on other tissues.

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Phomopsin may however be utilised in treatment of cancers other than liver cancer by selecting formulations or derivatives of phomopsin which enhance selectivity of the drug for certain types of cancer cells or certain types of cancers. Derivatives of phomopsins may be formed which are conjugates with monoclonal antibodies. The monoclonal antibody may be produced by known methods to provide selectivity for cancer cells.

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Phomopsins are characterised by a 13-member ring structure generally of formula I

Y OH

$$X \longrightarrow O$$
 R^1
 $C \longrightarrow R^2$
 $C \longrightarrow R^3$
 $C \longrightarrow R^4$
 $C \longrightarrow N \longrightarrow C$
 C

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wherein

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R1, R2, R3, R4, R5, R6 and R7 are optional substituents and may be independently selected from the group consisting of hydrogen, aliphatic, aromatic, peptide chains and halogen.

- X is aliphatic, hydrogen or halogen (preferably hydrogen); and Y is aliphatic, hydrogen or halogen (preferably chlorine); where present a peptide chain may be conjugated with a monoclonal antibody (Mab).
- The preferred phomopsins and phomopsin derivatives are those containing the group of formula Ia:

CI OH

OH

OR

$$R^{1}$$
 R^{6}
 R^{7}
 R^{-}
 R^{-

- In formula I and Ia R¹, R², R³, R⁵, R⁶ and R⁷ may typically be independently selected from hydrogen and aliphatic and R⁴ is generally a peptide. In one embodiment R⁴ is a peptide conjugated with an antibody, particularly a monoclonal antibody (Mab). More preferably R¹, R², R⁵ and R⁶ are lower aliphatic and R³ and R⁷ are hydrogen. Even more preferably R¹, R² and R⁶ are lower alkyl and R⁶ is lower alkyl or lower alkenyl. Most preferably R¹ is ethyl, R² is methyl, R³ is hydrogen, R⁵ is isopropyl or iso-propenyl and R⁶ is methyl. Where used herein the terms lower aliphatic, lower alkyl and, lower alkenyl include groups containing up to six carbon atoms and most preferably up to 4 carbon atoms.
- 30 The preferred stereochemistry of the compounds of formula Ia is as shown in formula Ib:

The group R⁴ is a peptide preferably a di- or tri-peptide which may be optionally bound to an antibody such as a monoclonal antibody. The preferred group R⁴ has the formula II:

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wherein the dotted line represents an optional double bond;

 ${\sf R}^8$ and ${\sf R}^9$ are independently selected from hydrogen and lower alkyl and more preferably ${\sf R}^8$ is methyl and ${\sf R}^9$ is ethyl;

R12 is selected from the group consisting of amino, mono substituted amino, disubstituted amino and an amino acid residue particularly the group of formula III:

$$HO_2C$$
 R^{13}
 $COOR^{15}$
 R^{14}

wherein R^{13} and R^{14} are hydrogen or together form a double bond and R^{15} is selected from the group consisting of hydroxy, amino, substituted amino or an antibody particularly Mab.

When R¹⁵ is an antibody or linked to an antibody it is preferred that R¹³ and R¹⁴ form a double bond providing a dehydroaspartic acid residue. A dehydroaspartic acid residue has been found to facilitate delivery of phomopsin via a Mab conjugate.

The carbon-nitrogen bond in the residue of formula III is relatively weak enabling an active phomopsin of formula Ia (wherein in the group of formula II R¹² is amino) to be released from the MAb once it becomes bound to cancer cells.

The most preferred phomopsin compounds are selected from phomopsin A, octahydrophomopsin A, iso-phomopsin and phomopsinamine A. These compounds have the formula set out below:

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In one aspect the invention provides a pharmaceutical composition for treatment of cancer, preferably liver cancer, containing a phomopsin compound or derivative thereof or pharmaceutically acceptable salt of the phomopsin or derivative and a pharmaceutically acceptable carrier.

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Salts of phomopsin such as the alkaline metal salts are reasonably water soluble. Aqueous solutions can be formed by dissolving the phomopsin in a dilute base such as sodium hydroxide to provide a neutral solution.

In another aspect the invention provides a method of treatment of a patient suffering cancer including administering to the patient a phomopsin compound or derivative thereof or pharmaceutically acceptable salt of the phomopsin or derivative.

The phomopsin compound may be administered by a variety of methods including oral administration in the form of a syrup, capsule, tablet or the like, by injection or by intravenous infusion.

Preferably the compound is administered by intravenous infusion

20 In a further aspect the invention provides the use of a phomopsin compound as hereinbefore described for preparation of a pharmaceutical composition for treatment of cancer and in particular liver cancer.

Phomopsin compounds are produced by certain fungi, including <u>Diaporte toxicus</u> (formerly <u>Phomopsis leptostromiformis</u>) and <u>Phomopsis emicis</u>, or may be derived from these natural products.

The isolation of phomopsin A is described by C. Culvenor, J. Edgar and M. Mackay, <u>Tetrahedron</u> Vol. 45, No. 8 pp 2351 (1989). Preparation of derivatives of phomopsins such as octahydrophomopsins are described by J. Edgar, J. Frahn, P. Cockrum and J. Culvenor in the paper "Lupinosis. The Chemistry and Biochemistry of the Phomopsins" <u>Mycotoxins and Phycotoxins</u>, collection of invited papers presented at the sixth International IUPAC Symposium on Mycotoxins and Phycotoxins, Pretoria, Rep. South Africa, 22-25 July 1985.

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The activity of phomopsin is believed to be due in part to the strong binding of the compound to tubulin. This may disrupt cell mitosis by inhibiting tubulin formation and cause depolymerization of formed microtubules. It may be preferred in some cases to use phomopsin in combination therapy with one or more other anticancer drugs or therapies. The drugs used in combination with phomopsin may be selected to enhance results by providing complementary activity in binding to microbubules. Examples of possible drugs for use in combination with phomopsin include paclitaxel, vinblastine, vincristine and alkaloids.

The present invention will now be more fully described with reference to the following examples. It should be understood, however, that the description following is illustrative only and should not be taken in any way as a restriction on the generality of the invention described above.

15 Example 1

The following data demonstrate, the anticancer activity of phomopsin A, octahydrophomopsin A, iso-phomopsin A and phomopsinamine A against 60 human cancer cell lines *in vitro*. Phomopsin A and octahydrophomopsin A were obtained by the method as described in the references referred to above.

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Iso-phomopsin A and phomopsinamine were prepared as follows:

ISOLATION OF PHOMOPSIN A

Background:

The extraction process is designed to minimise difficulty and cost. The fermented seed is continuously extracted with recycling 15% methanol:water through an in line XAD (styrene divinylbenzene copolymer) column. The time required for adsorption of phomopsin A onto the XAD is quite lengthy, but requires minimal operator input. The timing of this step is not critical, hence can be adapted to suite operating conditions.

The phomopsin A has a relatively low solubility in 15% methanol. The procedure relies on the adsorption of phomopsin A on the XAD resin driving the solubility equilibrium of phomopsin A in the fermented seed toward dissolution. This

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procedure reduces solvent usage, volumes to be handled and flammability hazards. The alternate method of extraction, without recycling would use 150+ litres of pure methanol for the initial extraction, involve a further concentration step (or dilution of the methanol extract to 900+L) then adsorption onto XAD. The current procedure uses 12 L methanol, requires minimal operation input for the adsorption phase and uses far less solvent (total volume 85L instead of 900+L).

The elution of the concentrated phomopsin A from the column is the first step in a 3 stage isolation to produce crystalline phomopsin A of 80-90% purity.

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Phomopsin may be eluted from the collection using 15% methanol as a preliminary wash and 100% methanol to complete elution. Silica gel flash column chromatography may be used for purification. The column is conditioned using 5:95 amonia:isopropanol and the concentrate dissolved in a minimum of 20:65:15 ammonia:isopropanol:water. Phomopsin is eluted using this 3 solvent combination. Recrystallisation from boiling glacial acetic acid provides phomopsin in 80-90% purity.

PREPARATION OF iso-PHOMOPSIN A

20 Materials:

0.05M HgCl₂:

280 mg HgCl₂ dissolved in 2 ml H₂O (+50 μ l 10M HCl).

Phomopsin A:

18.3 mg PhA dissolved in 2 ml H₂O (with puff of NH₃).

1M HCI

Method:

Phomopsin A (2.0 ml) was mixed with 0.05M HgCl₂ (1 ml) and 1M HCl (200 µl), total volume 3.2 ml, and left at room temperature for 5 hours. The solution was diluted to 8 ml then passed through a prepared C18 Maxi-clean SPE cartridge (900 mg) and washed with 7-8 ml H₂O. The Maxi-clean was then eluted with 8-9 ml MeOH and made to 10 ml. The aqueous eluate from the first C18 cartridge was reprocessed through a second C18 cartridge to check whether the first cartridge was overloaded. The MeOH eluate from the second cartridge had very little residue on drying and was not included in further processing.

The methanol eluate was evaporated to dryness and subject to HPLC analysis and preparative HPLC.

Needle contamination with mercuric chloride was enough to cause almost complete conversion to iso-phomopsin. A needle used for a solution containing mercuric chloride could not be used for phomopsin, even with exhaustive washing. The phomopsin - HgCl₂ reaction mixture could be pumped back and forth through a disposable needle (20-30 times), a sample removed for assay, and the remainder of the sample left at RT for 5 hours, with hourly sampling (if necessary).

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PREPARATION OF PHOMOPSINAMINE

Phomopsin A (15.3 mg) was dissolved in 1M HCl and left at RT for 28 hours. The reaction mixture was diluted to 8 ml then passed through a strong anion exchange cartridge (SAX, 600 mg) to remove any unreacted phomopsin A (pH of solution expected to be @ 1.52). The aqueous eluate (+ washings) was then passed through a prepared C18 cartridge (900 mg), washed with H_2O (10 ml) then eluted with methanol (10 ml).

The methanol eluate was evaporated to dryness subject to HPLC analysis and preparative HPLC.

This method may be modified by sampling the reaction mixture after 5-6 hours, 24 hours and 28-30 hours. All washings and eluates may be assayed by HPLC to monitor the conversion of phomopsin to phomopsinamine.

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The methods used are those employed by the United States National Cancer Institute (NCI) as a primary screen for discovering compounds with anticancer potential (Boyd and Paull, 1995). The data are presented in the standard format used by NCI to show, for each compound tested, the absolute and relative sensitivity of individual cancer cell lines to the compounds and to demonstrate reproducible and selective effects.

HOLLOW FIBER ASSAY FOR PRELIMINARY IN VIVO TESTING

The Biological Testing Branch of the Developmental Therapeutics Program has adopted a preliminary in vivo screening tool for assessing the potential anticancer activity of compounds identified by the large scale in vivo cell screen. For these assays, human tumour cells are cultivated in polyvinylidene fluoride (PVDF) hollow fibers, and a sample of each cell line is implanted into each of two physiologic compartments (intraperitoneal and subcutaneous) in mice. Each test mouse receives a total of 6 fibers (3 intraperitoneally and 3 subcutaneously) representing 3 distinct cancer cell lines. Three mice are treated with potential antitumor compounds at each of 2 test doses by the intraperitoneal route using a QD x 4 treatment schedule. Vehicle controls consist of 6 mice receiving the compound diluent only. The fiber cultures are collected on the day following the last day of treatment. To assess anticancer effects, viable cell mass is determined for each of the cell lines using a formazan dye (MTT) conversion assay. From this, the %T/C can be calculated using the average optical density of the compound treated samples divided by the average optical density of the vehicle controls. In addition, the net increase in cell mass can be determined for each sample as a sample of fiber cultures are assessed for viable cell mass on the day of implantation into mice. Thus, the cytostatic and cytocidal capacities of the test compound can be assessed.

Generally, each compound is tested against a minimum of 12 human cancer cell lines. This represents a total of 4 experiments since each experiment contains 3 cell lines. The data are reported as %T/C for each of the 2 compound doses against each of the cell lines with separate values calculated for the intraperitoneal and subcutaneous samples.

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Compounds are selected for further *in vivo* testing in standard subcutaneous xenograft models on the basis of several hollow fiber assay criteria. These include: (1) a % T/C of 50 or less in 10 of the 48 possible test combinations (12 cell lines X 2 sites X 2 compound doses); (2) activity at a distance (intraperitoneal drug/subcutaneous culture) in a minimum of 4 of the 24 possible combinations; and/or (3) a net cell kill of 1 or more cell lines in either implant site. To simplify evaluation, a points system has been adopted which allows rapid viewing of the activity of a given compound. For this, a value of 2 is assigned for each compound dose which results in a 50% or greater reduction in viable cell mass. The

intraperitoneal and subcutaneous samples are scored separately so that criteria (1) and (2) can be evaluated. Compounds with a combined IP+SC score \geq 20, a SC score \geq 8 or a net cell kill of one or more cell lines are referred for xenograft testing. These criteria were statistically validated by comparing the activity outcomes of > 80 randomly selected compounds in the hollow fiber assay and in the xenograft testing. This comparison indicated that there was a very low probability of missing an active compound if the hollow fiber assay were used as the initial *in vivo* screening tool. In addition to these criteria, other factors (e.g. unique structure, mechanism of action) may result in referral of a compound for standard xenograft testing without the compound meeting these criteria.

SCREENING DATA REPORT COMPONENTS

The Calculated Measurement of Effect: Percentage Growth (PG)

The measured effect of the compound on a cell line is currently calculated according to one or the other of the following two expressions:

If (Mean OD_{test} - Mean OD_{tzero}) ≥ 0 , then

 $\label{eq:pg} PG = 100 \ x \ (Mean \ OD_{test} - Mean \ OD_{tzero})/(Mean \ OD_{ctrl} - Mean \ OD_{tzero})$ If (Mean $OD_{test} - Mean \ OD_{tzero}) < 0$, then

PG = 100 x (Mean OD_{test} - Mean OD_{tzero})/Mean OD_{tzero}

20 Where:

Mean OD_{tzero} = The average of optical density measurements of SRB-derived color just before exposure of cells to the test compound.

Mean OD_{test} = The average of optical density measurements of SRB-derived color after 48 hours exposure of cells to the test compound.

25 Mean OD_{ctrl} = The average of optical density measurements of SRB-derived color after 48 hours with no exposure of cells to the test compound.

The Data Sheet:

This page of the data package represents the experimental data collected against each cell line. The first two columns describe the subpanel (e.g. leukemia) and cell line (e.g. CCRF-CEM) involved. The next two columns list the Mean OD_{tzero} and Mean OD_{ctrl} ; the next five columns list the Mean OD_{test} for each of five different concentrations. Each concentration is expressed as the log_{10} (molar or

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μg/ml). The next five columns list the calculated PGs for each concentration. The response parameters GI50, TGI, and LC50 are interpolated values representing the concentrations at which the PG is +50, 0, and -50, respectively. Sometimes these response parameters cannot be obtained by interpolation. If, for instance, all of the PGs in a given row exceed +50, then none of the three parameters can be obtained by interpolation. In such a case, the value given for each response parameter is the highest concentration tested and is preceded by a ">" sign. This practice is extended similarly to the other possible situations where a response parameter cannot be obtained by interpolation.

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Dose-Response Curves:

The dose-response curve page of the data package is created by plotting the PGs against the log₁₀ of the corresponding concentration for every cell line. The cell line curves are grouped by subpanel. Horizontal lines are provided at the PG values of +50, 0, and -50. The concentrations corresponding to points where the curves cross these lines are the G150, TG1, and LC50, respectively.

The Mean Graphs:

Mean graphs facilitate visual scanning of data for potential patterns of selectivity for particular cell lines or for particular subpanels with respect to a selected response parameter. Differences in apparent selectivity patterns may occur for the same compound against the same cell lines when different parameters are compared. The mean graphs page of the data package shows mean graphs at each of the principal response parameters: G150, TG1, and LC50. Bars extending to the right represent sensitivity of the cell line to the test agent in excess of the average sensitivity of all tested cell lines. Since the bar scale is logarithmic, a bar 2 units to the right implies the compound achieved the response parameter (e.g. G150) for the cell line at a concentration one-hundredth the mean concentration required over all cell lines, and thus the cell line is unusually sensitive to that compound. Bars extending to the left correspondingly imply sensitivity less than the mean. If, for a particular drug and cell line, it was not possible to determine the desired response parameter by interpolation, the bar length shown in either the highest concentration tested (and the listed log10 of the

response parameter will be preceded by a ">") or the lowest concentration tested (and the listed log_{10} will be preceded by a "<").

The values at either limited (> or <) are also calculated in the mean used for the mean graph. Therefore, the mean used in the mean graph may not be the actual mean of the G150, for instance. For this reason, we shall refer to this value as the MG-MID (for mean graph midpoint).

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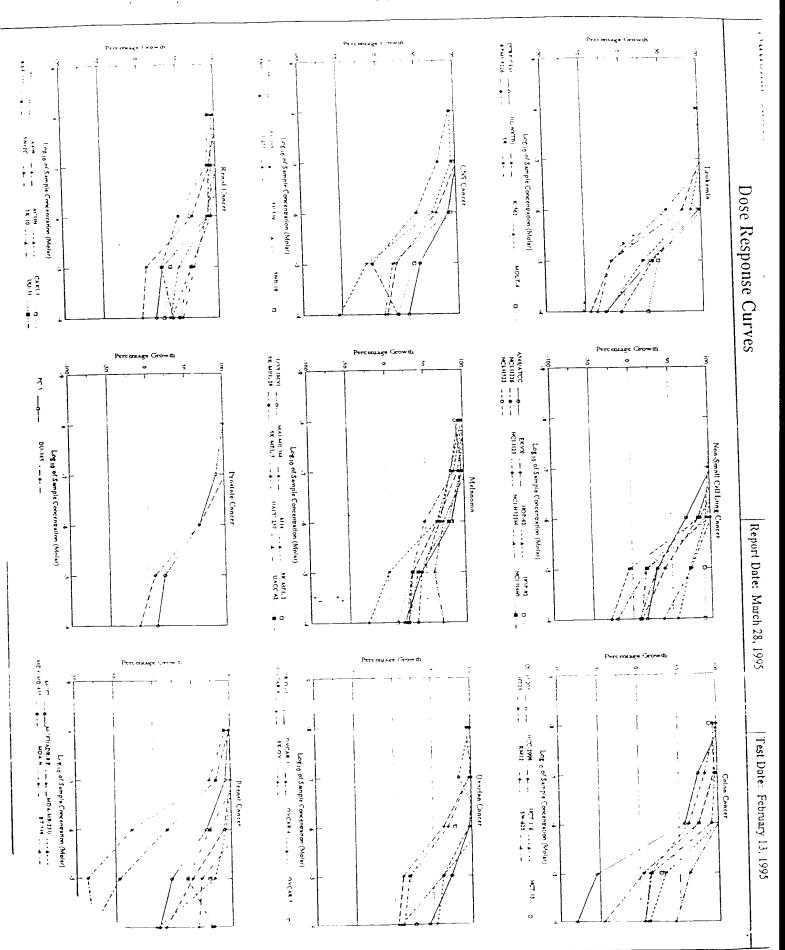
National Cancer I

titute Developmental Therapedics Program. In-Vitro Testing Results

Experiment ID: 9502RM16 Test Type: 8 Units: Molar
Port Date: March 28, 1995 Test Date: February 13, 1995 QNS: SHP MC:

DMI: Phomopsin A Stain Reagent: Dual-Pass SSPL: 0FLC

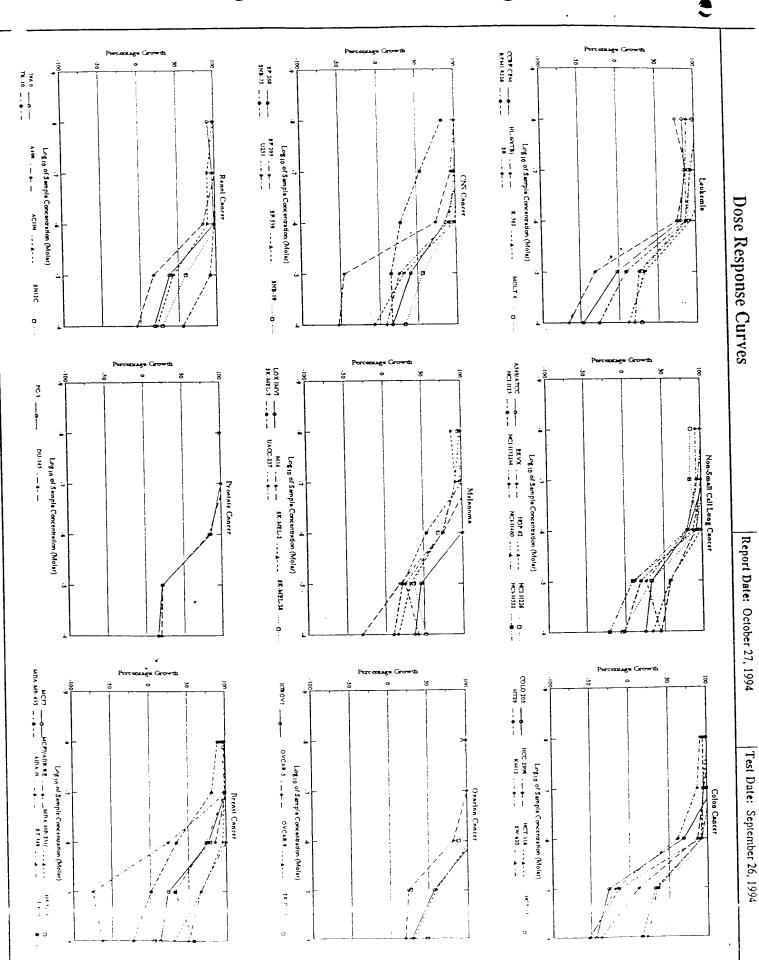
	Тапы					Log1(Concen	tietion	,						
Panel/Cell Line	Zerc	Ctil	- 6 C	n C⊊ tic -7.0	al Dens		_			cent (
Leukemia	2610		- c . c	- / . 0	-6.0	-5.0	-4.0	- 8 . 0	-7.0	-€.0	- 5 . C	-4.0	GISC	TGI	ucso
CCRF-CEM	0.634	1.663	1 649	1.745	1.640	0.979	0.479	9.0							
HL-60 (TB)	0.592		1.651		1.363	0.494	0.337	101	10 é	9.E	34	- 24	5,55E-0€	3.79E-05	1.00E-04
⊼-562	0.36?	1.209	1.161		1.101	0.560	0.394	97	101	67	-17 24	- 4 3	1.90E-06	6.62F~06	11 005 0.
MOLT-4		1.747	1.733	1.761	1.698	1.143	0.995	٥٥	103	95	43	~23 24	3.66106	3 24F-05	11 000 0.
RPMI-8226	0.735	1.450	1.531	1.516	1.472	0.992		111	109		36	-5	7.33E-06	>1.00E-04	>1.00E-04
SR	0.466	0.856	0.923	0.896	0.686	0.406		116	111	54	-16	-35	1 155 06	7.61E-05	>1.00E-04
Non-Small Cell Lun	g Cance										•	- 3 3	1.132-06	5.66E-0€	1.00E-04
AS49/ATCC		1.362	1.383	1.389	1.055	0.681	0.54€	102	103	6 ¢	31	1 7	3 145-06	>1.00E-04	
EKVX	0.402	0.935	0.946	0.966	0.854		0.461	102	10€	€ 5	4 5	1.	6.09E-06	1.00E-04	11.002-04
HOP-62	0.391	0.953	0.974	0.985		0.798	0.705	104	100	96	7.2	5.6	>1.00E-04	1.00E-04	11.00E-04
HOP-92 NCI-H226	0.761	1.260	1.329	1.350	1.309	1.217		114	116	110	٠,	ç -5	>1.00E-04	⇒1.00E-04	11.00E-04
NCI-H226		0.890 1.205		0.948	0.854	0.562		107	121	57	- 4	- 2 h	2.55E-06	9.03E-06	1.00E-04
NCI-H322H	0.624		1.246		1.214			105	102	101	74	3 ь	4.65E-05	>1.00E-04	21.005-04
NCI-H460	0.181		1.653			0.931		102	9 5	94	3.0	દ	4.92E-06	>1.00E-04	1.00E-04
NCI-H522		0.954		1.235	0.972	0.349	0.271	103	111	€ 3	16	ب	3.21E-06	>1.00E-04	>1.00F=04
Colon Cancer	0.415	0.234	0.500	0.963	0.952	0.513	0.32ε	103	105	100	16	-21	4.06E-06	2.97E-05	>1.00E-04
COLO 205	0.326	1.242	1 303	1.010	0 040	0 151	0.068								
HCC-299€	0.590	1.321	1 264	1.263	1 124	0.131	0.068	107	75	57	-54	-79	1.15E-06	3.26E-06	9.21E-06
HCT-116	0.161		1.209	1.263	1 245	0.621	0.319	95 9 7	95	74	4	-46	2.23E-06	1.21E-05	>1.00E-04
HCT-15	0.317	1.751	1.611	1.714	1 363	0.697		90	102	101	32	11	5.47E-06	>1.00E-04	>1.00E-04
HT29	0.166	0.659	0.622	0.636	0.796			95	97	74 91	26	10	3.23E-06	>1.00E-04	>1.00E-04
K0:0.2	0.294	1.232	1.230	1.07€	0.675	0.411		100	63	62	14	5	3.42E-06	>1.00E-04	>1.00E-04
SW-620	0.156	1.016	0.962		1.023			96	107	101	62	44	1./4E-06	>1.00E-04	>1.00E-04
CNS Cancer										101	01	• • •	4.302-03	>1.00E-04	>1.00E-04
SF-268	0.463	1.301	1.314			0.692		101	101	6.9	51	36	1 195-05	>1.00E-04	
SF-295	0.400		1.122		0.900			107	102	74	21	6	2 61F-06	>1.00E-04	>1.00E+04
SF-539		0.666			0.730			94	94	69	-16	-54	1.64E-06	6.17E-06	7 705-05
SNB-19 SNB-75		1.452			1.363		0.762	93	97	92	44	22	7.56E-06	>1.00E-04	>1.755-03
T251	0.361	0.626	0.610		0.500	0.339	0.432	93	77	4.8	-11	21	€.46E-07		>1.00E-04
Melanoma	0.159	0.853	0.E53	0.863	0.776	0.302	0.225	100	101	€ 9	16	4	3.40E-06	>1.00E-04	>1.00E-04
LOX IMVI	0 161	1.07€	0.000	3 050											
MALME-3H		0.952				0.574		90	97	52	43	2.0	€.71E-06	>1.00E-04	>1.00E-04
124	0.196		0.521	0.914		0.619		101	9.5	65	32	25	2.76E-06	>1.00E-04	>1.00E-04
SK-MEL-2	0 746	1.404		1.373	0.406 1.297			9ε	ē 3	64	C-	-27		1.04E-05	
SK-MEL-26	0.576	1.271			1.047			97	95	84	32	11		>1.00E-04	
SK-MEL-5	0.034		1.053		0.522			94 100	63 E7	6 E	44	37		>1.00E-04	
UACC-257	0.536				0.962	0.544	0.264	113	104	72	30 60	23		>1.00E-04	
WACC-62	0.577	1.790		1.735	1.533	1.043	0.547	101	104	70	36	70 26		>1.00E-04	
Owarian Cancer							4.00,	101		15	36	- C	5.17E-06	>1.00E-04	>1.00E-04
ICK-OV1	0.515	1.761	1.748	1.761	1.726	1.429	1.069	90	102	97	73	44	6 435-05	>1.00E-04	>1 005 04
OVCAR-3	0.293	0.611	0.620	0.79€	0.623	0.350	0.313	102	- 67	64	11	7,	1 625-06	>1.00E-04)1.00E-04
OVCAR-4	0.467	1.061	1.074	0.964	1.167	0.652	0.800	99	6.4	114	63	54	>1.00E-04	>1.00E-04	>1.00E-04
OVCAR-5 OVCAR-6	0.393			0.872		0.465	0.518	101	102	7 £	20	27	3.05E-06	>1.00E-04	>1 00E-04
\$E-0V-3	0.267	0.947	0.914	0.943	0.925	0.692	0.320	95	òċ	97	61	Ę	1.69E-05	>1.00E-04	>1.00E-04
Renal Cancer	0.466	0.975	0.002	0.961	0.621	0.565	0.525	104	ē.	7 C	16	11		>1.00E-04	
766-0	0.200	0.913	0.949	0 646	0 505	0 301									
A496			1.550			0.389		105	9(8 €	7.€	1 €		>1.00E-04	
ACHN		1.396	1 417	1.324	1.406		1.079	96 101	9:	67	6	Ć.		9.31E-05	
CAKI-1	0.466	0.940	0.691	0.85/	0.762	0.641		90	9 £	E 9	46	3 €		>1.00E-04	
RXF-393	0.704		1.469	1 436	1.113	0.913		90 91	6 t 6 7	63 4 9	37 25	2.6		>1.00E-04	
SN1.2C		1.274	1.312	1.309		0.950		104	104	92	64	3 6		>1.00E-04	
TK-10	0.627	1.221	1.166	1.227		1.032		94	101	65	68	3 E 5 3	3.41E-05	>1.00E-04	>1.00E-04
0 0-31	0.593	1.442	1.424	1.367		1.134		96	94	91	64	4 €	71.00E-04	>1.00E-04 >1.00E-04	>1.00E-04
rostate Cancer			•						-	- 1	04	4 (7.002-03	71.00E-04	>1.00E-04
PC-3	0.302	1.096	1.092	1.010	0.625	0.465	0.360	100	86	66	20	16	2 235-06	>1.00E-04	>1 00E=04
DO-145	0.339	1.061	1.122	1.073	0.617	0.396	0.296	106	102	66	8	-13		2.42E-05	
sreast Cancer								_			-		1.0.2	2.422.03	- 1.002-04
MCF7 MCF7/ADR-RES	0.423		1.156			0.563	0.465	96	92	€7	23	€.	2.33E-06	>1.00E-04	>1.00E-04
MOA-ME-231/ATCC	0.330	0.907		0.904		0.609		99	ōċ	90	4 E	13		>1.00E-04	
HS 576T		Q. 960 1.319	0.954		0.919			ة ق	101	93	77	1		>1.00E-04	
MDA-MB-435	0.864	4.329	1.337	1.350	1.324			104	107	101	71	75		>1.00E-04	
MDA-N	0.320	0.961 0.752	0.966		0.427			9.6	60	16	-46	-60		1.63E-06	
BT-549	0.214	0.752	0.715	0.59€	0.152			63	71	-50	-66	-76		5.11E-07	
T-47D	0.711		0.822		0.665	0.664	0.666	100	121	112	60	56		>1.00E-04	
		2.002	1.666	2.094	1-626	1.252	1.655	è J	107	71	4.2	73		>1.00E-04	1.00E-04

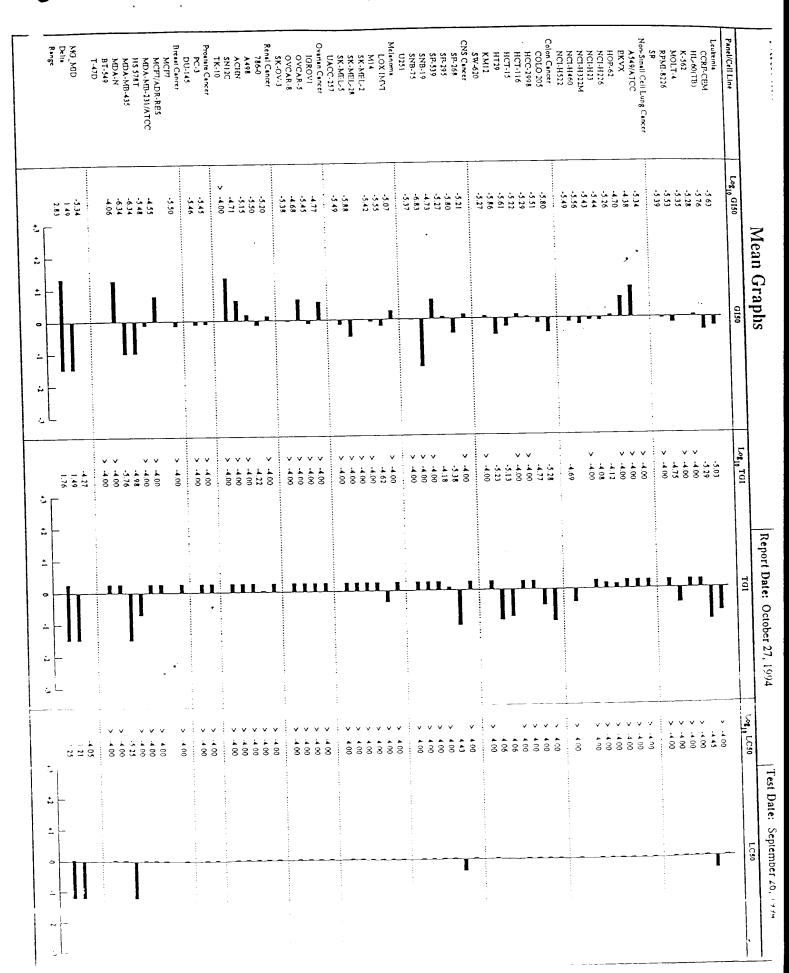


NO NO Pero Range	# 1410 # 140 # 140 F.	ACCT ACCT ACR RIS ACCA ACR DI ATTO ACS SPET	Property Control	11 A 11	AA9E CAXC.	Result see of	CALLON V	DVCAR I	0.400 (m. n.) (1400 (m.)	SX AFE	NING NO.	VENT XOT	1500 14 des 15 des	SF 310	198 ds (-ws) (-ws)	35 K F T T T T T T T T T T T T T T T T T T	HCT -	1 (1) (1) (1) (1) (1) (1) (1) (1) (1) (1	- 1 H 2 H 2 H 2 H 2 H 2 H 2 H 2 H 2 H 2 H	8	10.17.00	TRANS CO. OFF CASE	S P	14 (A)	CORT (1 +)	Panelly all I we	
324 1 55 2 79	3 4 (2) 4 (2)	300	363	28 7 1 2	18 5 5 5 7 7 5 5 5 5 5 5 5 5 5 5 5 5 5 5	378	3 4 3 S	2 7 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	3 29	327	3 3 3 3 3 8		3.03	 5 3 3 3	492	376		3.32				3 3 30 3 22	321 394	ند ه ام ا		0.517)	
			TT		11.		_}				.الـ		1	* T		1	Υ Υ `	Π						-*- _¥	Τ	(1150	
-4.24 2.05 2.29	> .6.29 > .4.23	* * * * * * * * * * * * * * * * * * *	× 4.8	> 4.00	2233	v .4.00	33 5 7 3 6 4 4 8	3888	v 4,8	× × × × × × × × × × × × × × × × × × ×	V 14.9%	, rg	× 1.03	× 3.22	88	× 7.88	× × × × × × × × × × × × × × × × × × ×	325	¥ 1.00	7 14 (B) 7 14 (B)	353	3 3 3	3.23	> 4.49	-4,42 -5,18	101 101	
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153 153 154	7 1 3 3 5 1 5 1 5 1 5 1 5 1 5 1 5 1 5 1 5	\$ 8 8 8 8 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	•	× 4.88	3388		38	333	× 1.8	838	338	38		3 - 7 7 -	88	33	38	333		333	33	388	7.8	888	333	17810 0000	17.00
													:	-												-	1000

C: D- 673162 -H / 0-1 / 2	Experiment ID: 9409SC89	Test Type: 8	Units: Molar
	Test Date: September 26, 1994	QNS:	MC:
port Date. October 20, 100	Stain Reagent: Dual-Pass	SSPL: OFLC	
MI: PHOMOPSIN A	Stam Reagent: Dum 1 and		

						10	Concentr	- B - L - O D							
				Optical	1 Densi		Concenci		Percer	nt Gr	owth				
	Time	Ctrl		-7.0	-6.0	-5.0	-4.0	-6.0 -	7.0 -	6.0 -	5.0 -	4.0	G150	TGI	LC 50
anel/Cell Line	Zero	CCLI	0.0						0.6	80	-2	-47	2.33E-06	9.40E-06	>1.00E-04
œukemia CCRF-CEM							0.132	84 75	86 88		_	-65	1.75E-06		3.56E-05
HL-60 (TB)							0.073 0.223		121	93	33	11	5.27E-06	>1.00E-04	:1.00E-04
K-562							0.560	96	93	90	26	28			1.00E-04
MOLT-4						0.247	0.144	103	94	67	-	-27	2.97E-06	1.78E-05	1.00E-04 1.00E-04
RPMI-8226						0.572	0.487	90	88	8.8	25	19	4 . 03E-06	31.00E-04	1.002-04
SR ion-Small Cell Lu									103	8.2	34	25	4 62E-06	>1.00E-04	1.00E-04
A549/ATCC	0.361	1.608	1.696		1.386	0.762	0.678	107 107	99	92	56	45	4 - 20E - 05	>1.00E-04	>1.00E-04
EKVX						1.239	1.117	100	114	99	57	35			>1.00E-04
HOP-62					1.635 0.961	0.720	0.564	87	85	96	34	- 5			>1.00E-04
NCI-H226					1.417	0.674	0.447	101	101	88	20	-2			>1.00E-04 >1.00E-04
NCI-R23	0.455 0.556				1.178	0.765	0.899	93	93	80	27	44	2.75E-06)1.00E-04	>1.00E-04
NCI-H322M NCI-H460		1.089		1.049	0.913	0.324	0.235	101	95 102	80 93	12 9	-21	3.27E-06	2.04E-05	>1.00E-04
NCI-H522		1.047	1.062	1.062	1.004	0.492	0.343	102	102	23	,	-21	3.2.2	•	
Colon Cancer					0 750	0.152	0.116	وو	108	69	-27	-44	1.58E-06	5.24E-06	>1.00E-04
COLO 205	0.206	0.993	0.985	1.055 0.808	0.750	0.132	0.164	104	96	87	11	-37	3.09E-06	1.66E-05	>1.00E-04
HCC-2998	0.262	0.831 1.467	0.855 1.507	1.415	1.405	0.631		102	94	93	32	15	5.08E-06	>1.00E-04	>1.00E-04 >1.00E-04
HCT-116	0.230 0.717	2.648	2.880	2.825	2.910		1.035	102	99	103	35	15 -52	6.07E-06	7 39F-04	6.68E-05
HCT-15	0.148	0.784	0.753	0.754	0.730	0.128	0.071	95	95 87	92 61	-14 -19	-52	1 38E-06	5.85E-0	6.72E-05
HT29 KM12	0.907	2.630	2.493	2.409	1.963	0.738	0.435	92 104	104	93	34	22	5.39E-06	>1.00E-0	>1.00E-04
SW-620	0.140	0.747	0.774	0.773	0.703	0.349	0.274	104	104	22			-		
CMS Cancer				1.132	0.994	0.660	0.486	104	106	87	40	16	€.20E-06	>1.00E-0	4 >1.00E-04
SF-268	0.367	1.090	1.120	1.263	1.111	0.302	0.258	100	94	74	-45	- 53	1.59E-06	4.16E-0	6 3.70E-05
SF-295	0.554 0.517	1.306	1.539	1.568	1.526	0.844	0.481	99	102	98	32	-7 33	5.31E-06	0.01E-0	5 >1.00E-04 4 >1.00E-04
ST-539 SNB-19	0.587	1.730	1.744	1.709	1.662	1.231	0.961	101	98 55	94 28	56 15	16	1.63E-07	>1.00E-0	4 >1.00E-04
SNB-19 SNB-75	0.367	C.848	0.767	0.629	0.502	0.440	0.444	63 103	98	28 91	26	40	4.23E-06	>1.00E-0	4 >1.00E-04
U251	0.191	0.840	0.862	0.830	0.781	0.357	0.247	103	50						
Helanoma			1.180	1.243	1.164	0.689	0.611	101	108	100	46	37	8.46E-06	>1.00E-0	4 >1.00E-04
TOX IMAI	0.279 0.250	1.168	0.617	0.657	0.530	0.320		66	110	76	19	-31	2.82E-0	2.38E-0	5 >1.00E-04 4 >1.00E-04
H1.4	0.250	1.464	1.350	1.395	1.232	0.855		67	92	74	32	16 51	3.80E-0	51.00E-0	4 >1.00E-04
SK-MEL-2 SK-MEL-28	0.305	0.827	0.804	0.816	0.664		0.573	96 106	98 101	69 54	37 22	10	1.32E-0	6 >1.00E-0	4 >1.00E-04
SK-MEL-S	0.354	1.728	1.806		1.094	0.656		98	92	75	26	42	3.23E-0	6 >1.00E-0	4 >1.00E-04
UACC-257	0.709	1.849	1.826	1.759	1.565	1.004	1.105	,,,			-				
Ovarian Cancer		1.442	1.490	1.646	1.535	0.968	0.646	104	119	109	57	27	1.70E-0	5 >1.00E-0	4 >1.00E-04
IGROVI	0.346				0.798		0.475	99	100	8.2	24	19	3.55E-0	6 >1.00E-0	14 >1.00E-04 14 >1.00E-04
OVCAR-5 OVCAR-8	0.550				2.519			105	133	104	59 26	30 47	4 198-0	6 >1.00E-0	4 >1.00E-04
sk-ov-3	0.423			0.940	0.826	0.543	0.637	94	114	0 =	20	• ,			
Renal Cancer					1.865	0.988	0.686	91	97	98	38	17	6.30E-0	6 >1.00E-0	4 >1.00E-04
786-0	0.434							99	100	83	17	- 5	3.19E-0	6 6.00E-0	05 >1.00E-04
A498	0.561 0.306							98		90	43	21	7.03E-0	6 >1.00E-0	04 >1.00E-04 04 >1.00E-04
ACHN SN12C	0.636							105		103	59 92	28 55	1.9/6-0	4 31 00E-	04 >1.00E-04
TX-10	0.399				1.037	0.996	6 0.757	100	106	9.6	92	23	J1.00E-0	71.002	
Prostate Cancer							3 1.322	99	100	86	21	15	3.58E-0	6 >1.00E-	04 >1.00E+04
PC-3	0.952							وَ وَ		63	22	20	3.46E-0	6 >1.00E-	04 >1.00E-04
DO-145	0.459	1.630	1.615	1.686	1.434										04 >3 005-04
Breast Cancer	0.259	9 1.243	1.224	1.244	1.009	0.48		98		76		12	3.13E-0	06 >1.00E-	04 >1.00E-04
MCF7 MCF7/ADR-RES				1.497	1.351			97				3.0	2 BAT-1	15 >1.00E-	04 >1.00E-04
MOA-ME-231, A				1.663	1.636			113					3.332-3	e Filode-	64 31,00E-04
HS 578T	0.58	6 1.199											4.57E-0	07 1.05E-	05 >1.00E-04
MDA-MB-435	0.28		4 , 1.160 2 1.440							2.3			4 . SBE -	07 1.73E-	06 5.58E-06
MDA—N ·· BT-544	0.33 c.60		_				5 0.890	: ^ -		100		40	ם יידר פ	ue >1 UUE-	04 >1 00F=04 64 33 00F=64
51-544 T+47D	6.77			1.32						·		7.7		2.77	

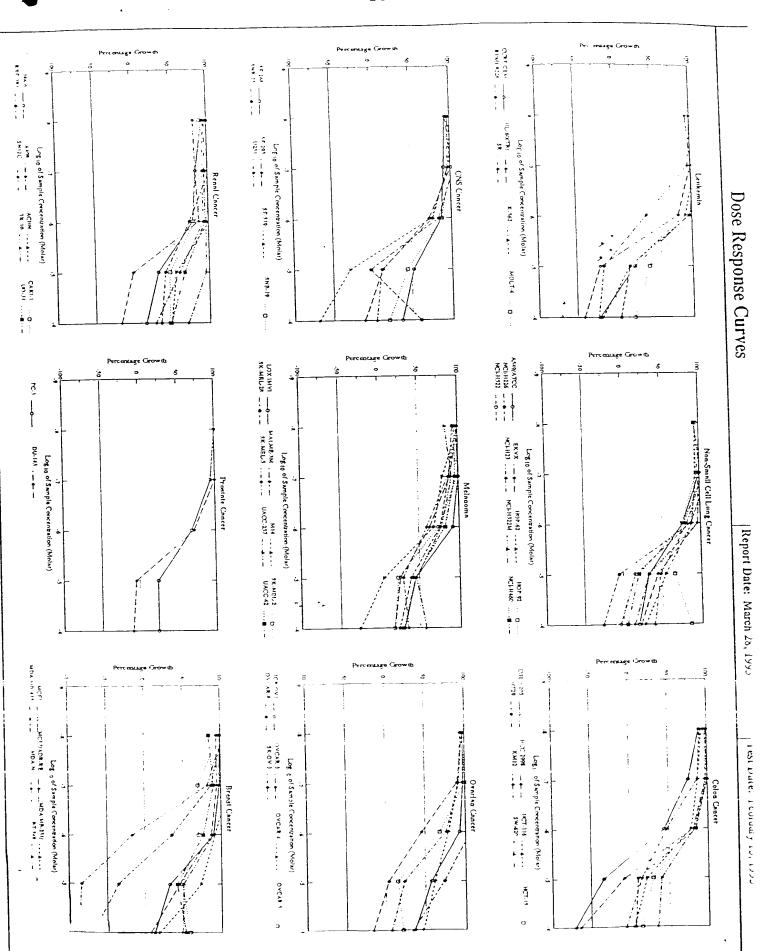


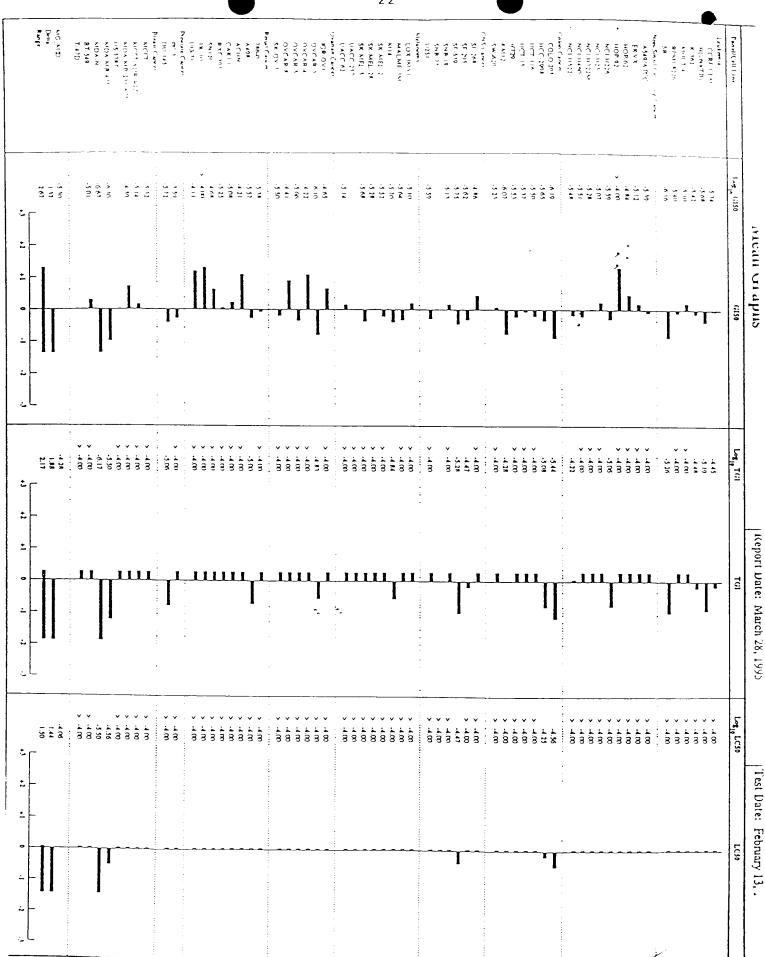


Experiment ID: 9502RM16 Test Type: 8 Units: Molar bort Date: March 28, 1995 Test Date: February 13, 1995 QNS: SHP MC:

MI: Iso-phomopsin A Stain Reagent: Dual-Pass SSPL: 0FLC

							Concenti	ac ion	Perce	.n. C	rout to				
	Time	_ ,		Op. tical	Emensit €.0 -	1 e s 5.0	- 4 .0	-6.0 -	7.C -	-6.0	- 5 . c	-4.C	G150	761	1.050
anel/Cell Line	Zero (Itil -	- 0.9-	-7.0 -	C. 0 -	3.0	• • •						4 5 45 06	3 558-05	>1.00E-04
eukemia CCRF-CEM	0.634	1.762	1.792				0.502		10€ 10€	97 63	25 -19	-21 -41	2.102-06		>1.00E-04
HL-60 (TB)							0.351		104	92	19	-17	3.76E-06	3.34E-05	>1.00E-04
K-562		1.370 : 1.845 :	1.372 : 1.670 :		.662 1		0.965	102	100	101	44	24	7.96E-06	>1.00E-04	>1.00E-04
HOLT-4	0.688		1.671		.567	.696	0.788		11C	97	19	-22	4.02E-06	5 44F=06	>1.00E-04 >1.00E-04
RPMI-6226 SR	0.486	1.032	1.031	1.013	.711	.414	0.377	100	9€	41	-15	- 22			
ion-Small Cell Lur	ng Cancer		1.374		.120), 6 92	0.556	104	100	77	3.3	7 è	4.11E-06	>1.00E-04	1.00E-04
A549/ATCC	0.3//					5.677	0.53€	94	101	9€	44	3.2	7.61E-06	>1.00E-04	>1.00E-04 >1.00E-04
EKVX HOP-62			0.664	0.663 (0.529	94	9.4	89 76	54 66	2.6 6.6	>1 00504	>1.00E-04	>1.00E-04
HOP-92						0.995 0.573	1.066	96 114	110	8.8	-6	-27	2.55E-06	£.73E-06	>1.00E-04
NCI-H226						0.373	0.709	104	105	83	4 E	39	€.51E-06	>1.00E-04	>1.00E+04
NCI-H23						0.926	0.752	106	96	96	32	1.4	5.26E-06	>1.00E-04	>1.00E-04 >1.00E-04
NCI-H322H NCI-H460	0.161			1.314	1.035	0.393	0.228	93 101	105 97	79 66	20 15	- 4 - 4	3.07E-06	6.00E-05	>1.00E-04
NCI-H522	0.413	1.073	1.081	1.050	0.992	0.514	0.395	101	51	•	10	•			
Colon Cancer		1.333	1.236	1.089	0.770	0.217	0.097	90	76	44	-34	-70	6.44E-07	3.66E-06	3 2.75E-05 5 5.66E-05
COLO 205				1.246	1.142	0.545	0.214	3 9	97	£2	−£ 21	-64 4			>1.00E-04
RCC-2996 RCT-116		1.304	1.227			0.406	0.211	93 97	6 E 9 B	-79 ě 5	22	14			>1.00E-04
HCT-15	0.317					0.711 0.233	0.512 0.207	وَهِ	100	€5	10	6			>1.00E-04
HT29	0.166 0.294	0.631	0.824 1.343			0.464	0.277	91	67	47	15	-6			5 >1.00E-04 1 >1.00E-04
KH1.2 SW-620	0.156	0.691	0.670			0.450	0.410	97	ة ة	€3	40	3 5	5.832-00	J1.00E-0.	71.002-04
CNS Cancer						0.966	0.617	94	92	8.6	52	37	1.365-05	>1.002-0	\$ >1.00E-04
SF-266	0.463	1.431				0.479	0.356	95	100	73	12		2.36E-06	3.37E-0	5 >1.00E-04
SF-295	0.400 0.367	1.038 0.660	0.867		0.745	0.275	0.123	101	97	76	-29		1.762-06	5.28E-0	6 3.41E-05 4 >1.00E-04
SF-539 SNE-19	0.571	1.365	1.360	1.362		0.930	0.733	97 97	100	8 9 8 4	44 -3				>1.00E-04
SNB-75	0.361	0.626	0.619		0.568	0.370	0.529 0.226	9.6	96	77	11		2.55E-0	>1.00E-0	4 >1.00E-04
U251	0.199	0.893	0.676	0.867	0.736	0.270	0.220								4 >1.00E-04
Melanoma LOX IMVI	0.191	0.962	0.963	0.980	0.921	0.551	0.430	96					2 315-0	5 31.00E-0	4 >1.00E-04
HALME-3H	0.464	1.037	1.039	0.976	0.631	0.611	0.563 0.146	100	23 03				1.982-0	5 1.45E-0	5 >1.00E-04
M3.4	0.196	0.569	0.571	0.496	0.453	0.215		94	99	75			3.C1E-0	5 >1.00E-0	4 >1.00E-04
SK-MEL-2	0.746	1.368	1.331	1.114	1.043	0.617	0.721	93					5.22E-0	6 >1.80E-0	4 >1.00E-04 4 >1.00E-04
SK-MEL-26 SK-MEL-5	0.034	1.014	1.006	0.685	0.622	0.320		9.9 6.4						>1.00E-0	4 >1.00E-04
UACC-257	0.536	1.297	1.175	1.234	1.133	0.885		96					7.21E-0	6 >1.00E-0	4 >1.00E-04
DACC-62	0.577	1.862	1.608	1.610	1.639	1.250	0.240				_			. >3 00E=0	4 >1.00E-04
Ovarian Cancer IGR-OV1	0.515	1.689	1.661	1.656	1.605	1.192		96				6 36 3 -17	7 675-0	7 1.47E-0	5 >1.00E-04
OVCAR-3	0.293	0.905	0.886	0.846	0.572	0.314		97 97			-		6 05F ± 0	5 >1.00E-0	04 >1.00E-04
OVCAR-4	0.467	1.176	1.151	1.121	1.026	0.467		رَةٍ وَ			6 1	5 21	2.202-0	6 >1.00E-0	04 >1.00E-04
OVCAR-5 OVCAR-6	0.393	0.867	0.672		1.252	0.950	0.583	106					3.93E+0	6 >1.00E=0	04 >1.00E-04 04 >1.00E-04
SK-OV-3	0.468		0.962	0.966	0.882	0.595	0.503	9 5	9 9 2	<i>2</i> /	υ 2	, 0			
Renal Cancer			0.901	0.629	0.794	0.442	0.317	94	4 64	4 7		2 16	4.19E-0	6 >1.00E-	04 >1.00E-04
766-0	0.200				1.371	1.079	0.903	8.			•	0 -16	2.675-0)6 9.94E-	06 >1.00E-04 04 >1.00E-04
A496 ACHN	0.406		1.471	1.547	1.470	0.993		10:				6 45	t 525-1	16 31 OOF-	04 >1.006-04
CAKI-1	0.466	0.950	0.904		0.862	0.695		10			-	2 35		16 11 OOF-	04 >1_00£-04
RXF-393	0.704				1.361	0.95		و	5 9	3 9		i1 2ε	2.11E-	05 >1.00E-	04 >1.00E-04 04 >1.00E-04
SN12C TK-10	0.371				1.07€	1.07	0.956	10		-		6 71 57 46	7 FIF-	05 >1.00E-	04 >1.00E-04
υο-31	0.593				1.439	1.16	6 1.016	9	7 9	.6 >	, ,	, 40			
Prostate Cancer					0.692	0.50	4 0.503	10	0 9	4 6	56	23 23	2.56E-	06 >1.00E-	04 >1.00E-04
PC-3	0.302			1.115						0 -	2	-5 -9			06 >1.00E-04
DU-145 Breast Cancer	0.35	1.02.	1.0.	1.020						8 !	90	32 12	4.845-	06 >1.00E-	-04 >1.00E-04
MCF7		Z.139		1.123	1.068		9 0.509 0 0.37E	-				44 7			
MCF7/ADR-RES		0 1.03					6 0.502	ءِ ج	7 11	0	92	73 16	2.60E-	05 >1.00F	-04 >1.00E-04
MDA-ME-231/2 HS 578T	0.40 0.86		6 1.391			1.11	9 1.174	ءِ ا				46 58 35 -69		07 3 137	-06 2.76L-UD
MDA-MB-435	0.32			4 1.164	0.€53							84 - 61			
MDA-N	0.21			4 0.654	0.179				52	9 E	ē0	50 41	5 S.72E.		-04 >1.00E-04 -04 >1.00E-04
BT-549 T-47D	0.47			5 0.600 7 2.015	1.810					90	76	41 5	2	. >1.00£	-04 /1.000 **
1-470	0.71														





D. 3164-J/0-1/4	Experiment ID: 9409SC89	Test Type: 8	Units: Molar
	Test Date: September 26, 1994	QNS:	MC:
	Stain Reagent: Dual-Pass	SSPL: OFLC	

							Concent	ration	Perce	nt Gr	owth				
	Time	~ · · ·		~7.0	l Densi -6.0	-5.0	-4.0	-8.0 -				4.0	GI 50	TGI	LC50
el/Cell Line	Zero	Ctrl	-0.0	,					_		-		3_12E-06	3 365-05	>1.00E-04
.kemia CCRF-CEM	0.250	0.846	0.867				0.143	103	9.7 9.8	98		-43 -59	2.39E-06	5.69E-06	4.99E-05
HL-60 (TB)	0.213						0.086	106 126		112	25	- 5 -		>1.00E-04	
K-562	0.129						0.159			106	46	5		:1.00E-04	
HOLT-4	0.261						0.168		104	67		-14			·1.00E-04
RPMI-8226	0.196					0.609	0.307	÷6	ōč	94	26	5	4.67E-06	>1.00E-04	.1.00E-04
SR 1-Small Cell Lun		r						104	103	90	31	11	4 76E-06	>1.00E-04	1.00E-04
A549/ATCC	0.361	1.402					0.476	104	101	98	64	5.6	>1.00E-04	>1.00E-04	1.00E-04
EKVX	0.668			1.712			1.022	95	6.2	79	53	21			1.00E-04
HOP-62	0.534	1.738		0.906			0.500	95	93	110	39	-15			1.00E-04 1.00E-04
NCI-H226 NCI-H23	0.455			1.630			0.636		105	93	37	16 51	5.93E-06		1.00E-04
NCI-H322M	0.556		1.351	1.395		0.840	0.986	95	100 9€	e 5 e 5	34 7	-30	2.84E-06		>1.00E-04
NCI-H460	0.219	1.062		1.025		0.281	0.150	95 100	56	و ج	10	-76	3.40E-06		5.00E-05
NCI-H522	0.434	1.0€5	1.065	1.059	1.034	0.500	0.104	100							
lon Cancer	0.206	0.975	0.991	1.024	0.792	0.114	0.109	102	10€	76	-45	-48	1.64E-06		>1.00E-04
COLO 205 MCC-2998	0.262	0.673	0.848	0.866	0.826	0.356	0.171	96	ي و	92	15	-35	3.55E-06		>1.00E-04 >1.00E-04
HCT-116	0.230	1.417	1.419	1.549	1.405	0.583	0.300	100	111 102	99 102	30 40	6 16	6.95E-06	>1.00E-04	>1.00E-04
HCT-15	0.717	2.847	2.851	2.880	2.893	1.573	1.050	100 98	96	93	-30	-26	2.24E-06	5.68E-06	>1.00E-04
HT29	0.145	0.617	0.806	0.804	0.774	0.611	0.283	116	9 €	62	-33	-69			3.02E-05
ED:CL2	0.907	1.983	2.156 0.683	0.687	0.618	0.269	0.149	99	99	87	23	2	3.82E-06	>1.00E-04	>1.00E-04
SW-620	0.140	0.650	0.005	0.00.	••								7 015 06	>1 00F=04	>1.00E-04
S Cancer SF-268	0.367	1.294	1.313	1.235	1.173	0.792	0.651	102	94 93	67 68	46 -36	31 -52	7.91E-06	5.12E-06	7.57E-05
SF-295	0.554	1.239	1.239	1.193	1.158	0.354	0.267	100 96	95	€2	28	- 52	3.91E-06	>1.00E-04	>1.00E-04
SF-539	0.517	1.466	1.449	1.435	1.309	1.230	1.007	100	9.6	89	57	37			>1.00E-04
SNB-19	0.567	1.709 0.601	1.709 0.730	0.810	0.627	0.466	0.523	84	102	106	23	36	4.72E-06	>1.00E-04	>1.00E-04
SNB-75	0.191	0.674	0.852	0.829	0.755	0.293	0.152	97	93	63	15	-20	3.03E-06	2.65E-05	>1.00E-04
U251 -lanoma	0.131							99	9€	91	43	19	7 22E-06	>1.00E-04	>1.00E-04
LOX IMVI	0.279	1.142	1.136	1.108	1.061	0.653	0.444	76	£1	46	-6	-56	7.86E-07	7.74E-06	5 7.13E-05
HG. 4	0.250	0.509	0.452 1.349	0.456	0.370 1.191	0.705	0.166	100	95	80	18	C	3.06E-06	>1.00E-04	>1.00E-04
SK-MEL-2	0.563	1.347 C.940	0.894	0.906	0.800	0.602	0.577	93	95	78	47	43		>1.00E-04	>1.00E-04 >1.00E-04
SK-MEL-26 SK-MEL-5	0.354		1.666	1.591	0.613	0.347	0.370	117	110	41	-2 20	1 27	7.37E-07		4 >1.00E-04
UACC-257	0.709		1.918	1.889	1.751	0.960	1.035	3.6	9€	85	20	2,	3.402 00	, ,11,000	
rarian Cancer					1 420	0.914	0.660	105	10€	94	49	27	9.72E-06	>1.00E-0	4 >1.00E-04
IGROV1	0.346		0.970	1.561	1.429	0.548	0.523	102	100	95	30	25	4.87E-06	>1.00E-0	4 >1.00E-04
OVCAR-5 OVCAR-8	0.377		2.695	2.769	2.718	1.919	1.214	103	107	105	66	32	2.95E-05	>1.001-0	4 >1.00E-04 4 >1.00E-04
SK-OV-3	0.423		0.882	0.666	0.802	0.530	0.57€	105	10€	86	24	3.5	3.862-04	J1.00E-0	
enal Cancer						0.992	0.760	93	94	99	40	24	6.82E-0	6 >1.00E+0	4 >1.00E-04
786-0	0.434			1.743	1.613	0.634	0.572	97	93	95	21	3	4.04E-0	6 >1.00E-0	4 >1.00E-04
A498	0.561		0.908	1.125	1.087	0.701	0.467	101	95	91	46	21	6.02E-0	6 >1.00E-0	4 >1.00E-04 4 >1.00E-04
ACHN SN1 2C	0.500		1.687	1.655		1.306	0.884	102	ōċ	101	€5 67	24 58	2.36E-0	5 31.00E-0	4 >1.00E-04
TK-10	0.399			1.090		0.981	0.789	101	103	101	67	56			
rostate Cancer							1.382	101	10€	€5	28	18	4.11E-0	6 >1.00E-0	4 >1.00E-04
PC-3	0.952					1.625		106	111	97	16	5	3.77E-0	6 >1.00E-0	4 >1.00E-04
DO-145	0.459	1.560	1.627	1.670	1.520	0.050						_		6 - 1 OOF O	4 51 DOE=04
reast Cancer MCF7	0.259	9 1.163	1.204	1.109	0.900	0.442		102	92	69	20	3	2.46E-0	6 31.00E-0	4 >1.00E-04 4 >1.00E-04
MCF7/ADR-RES	0.517		1.347	1.375	1.266			106		95 107	19 64	2 26	2.35E-0	5 >1.00E-0	4 >1.00E-04
MDA-MB-231/AT		1.660				1.286		102 103	10C		36	31	4.03E-0	6 >1.00E-0	4 >1.00E-04
HS 578T	0.56	6 1.116				0.786		96			-20	3	1.25E-0	6 .	>1.00E-04
MDA-MB-435	0.283					0.310			92				6.90E-0	7.30E-0	06 >1.00E-04 04 >1.00E-04
MDA-N BT-549	0.60					1.026	0.794						3.44E-0	15 21.00E-0	04 >1.00E-04
T-47D	0.77		2.196			1.353	1.352	104	9€	103	42	4.2	1.40E-0	,1.002 (
-															

Dose Response Curves

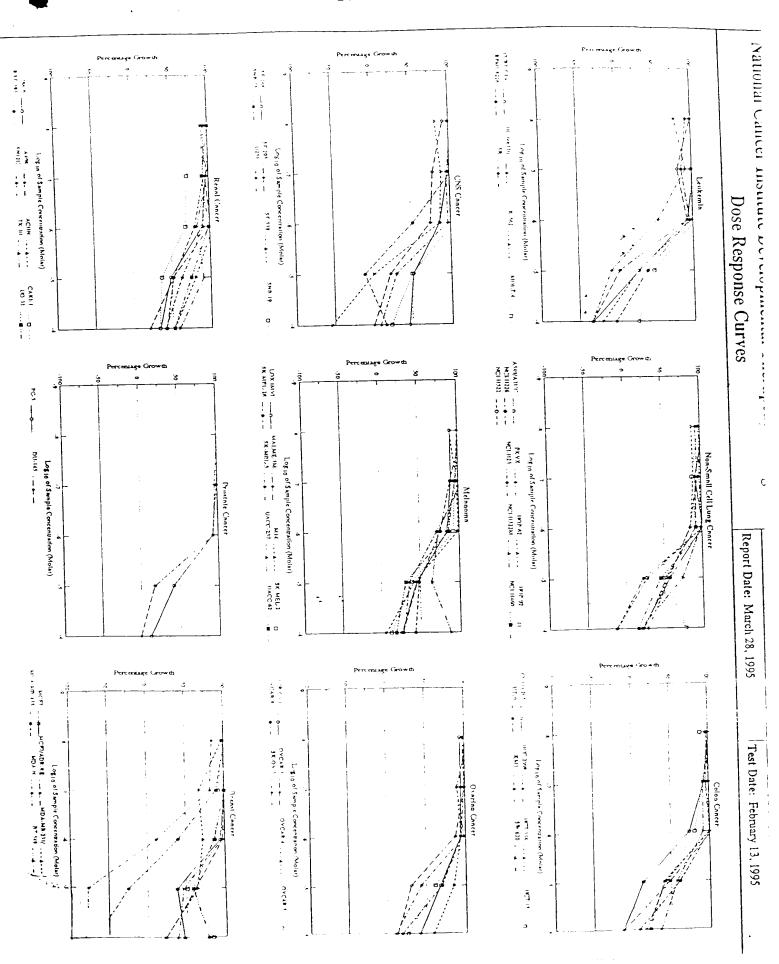
Report Date: October 27, 1994

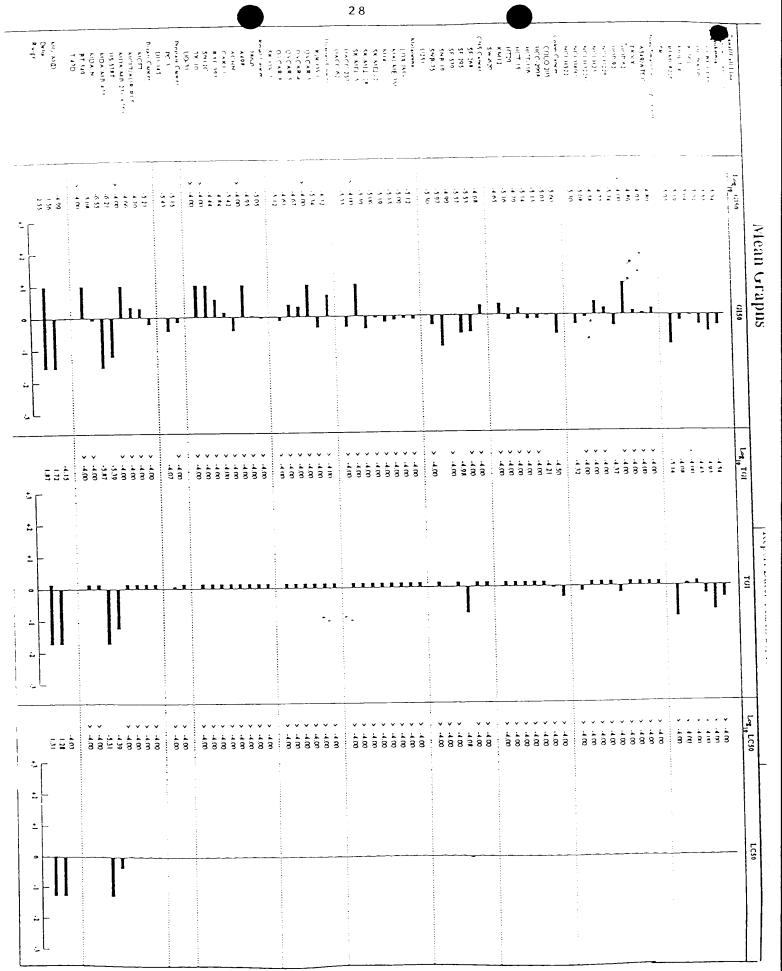
Test Date: September 20, 1994

MO_MID Delia	MDA-MD-435 MDA-N BT-349 T-47D	Breat Cancer MCF7/ADR:RES MCF7/ADR:RES MDA-MB-231/ATCC HS 578T	Prointe Carcer PC-3 DU-145	Renal Cancer 786-0 A498 ACPO SN12C TK-10	Overlan Cancer IGROV1 OVCAR-5 OVCAR-8 SK-OV-3	Melanoma LOX IMVI MI4 SK-MEL-28 SK-MEL-28 SK-MEL-5 UACC-257	CNS Clarker SP-268 SP-295 SP-359 SP-559 SNB-19 SNB-75 U251	Colon Cancer COLO 205 HCC-2998 HCT-116 HCT-15 HCT-15 HCT-15 KM12 SW-620	Non-Small Cell Lung Cascer A549/ATCC EKVX HOP-62 NCT-H226 NCT-H23 NCT-H23 NCT-H250 NCT-H260 NCT-H261	Leutemia CCRP-CEM HL-80(TB) K-562 K-562 MOLT-4 RPM-8226 SR	Panel/Cell Line
-529 0.87 2.16	5.13 5.16 5.17 5.17 5.17 5.17 5.17 5.17 5.17 5.17	3.4.5.5.5.5.5.5.5.5.5.5.5.5.5.5.5.5.5.5.	-5.39 -5.42	> -1.00 > -1.00	-5.01 -5.31 -4.53 -5.41	-5.14 -6.10 -5.51 -5.10 -5.46	-5.41 -5.41 -5.33 -5.53	-5.79 5.45 -5.29 -5.16 -5.83 -5.83	× 4.00 × 4.00 × 4.00 × 4.00 × 4.00 × 5.15 × 5.15	.5.51 .5.62 .5.29 .5.06 .5.57	150 C150 C150
1.10	-5.14 >-4.00 >-4.00	V 400	> 4.00 > 4.00	> 4.00 > 4.00 > 4.00 > 4.00 > 4.00	> 4.00 > 4.00 > 4.00 > 4.00 > 4.00	V 4.00 V 4.00 V 4.00 V 4.00	> 4.00 -5.29 > 4.00 > 4.00 > -4.00 -4.58	-5.37 -4.69 > -4.00 > -4.00 -5.25 -5.24 > -4.00	> 4.00 > 4.00 > 4.00 > 4.00 > 4.00 > 4.00 - 4.81 - 4.88	4.86 -5.23 > -4.00 > -4.00 > -4.00 > -4.00	L0810 T01
		_111								<u> </u>	TG1
349	v 400	7 / V V V V S 3 3 3 3 8 8	v v 400	> 400 > 400 > 400	> 4.00 > 4.00	V 1433 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	4.12 • 4.00 • 4.00 • 4.00 • 4.00	0 00000	v v v v v v v v v v v v v v v v v v v	> 1.00 > 1.00 > 1.00 > 1.00 > 1.00	Cog 10 T C 20
-						•		1	1	-	LC50

Experiment ID: 9502RM16Test Type: 8Units: MolarPort Date: March 28, 1995Test Date: February 13, 1995QNS: SHPMC:DMI: Octahydrophomopsin AStain Reagent: Dual-PassSSPL: 0FLC

						10010	Concents	ation							
	Time		Bean	Optical	Densi	ties				nt Gr				- · ·	1 0
Panel/Cell Line	2erc	Ctrl	-€.0	-7.0	-6.0	-5.0	- 4 . C	- E . C -	7.C -	6.6 -	5.0 -4		5: 50		ವಿಕ ೩ ೧
Leukemia	0.63≮	1.663	1.656	1 663	1.595	0.922	0.423		102	9-3		- 3-3			≥1.00E-04
CCRF-CEM HL-60 (TB)			1.633	1.440	1.562		0.369	100	٤١	9.3		- 3.4	2.96E-Cc	1.175-15	11.00E-04 21.00E-04
K-562	0.362	1.209	1.242	1.20€		0.606	0.303	104	100	9 e 103	27 -	·21 26	4.62E-06		>1.00E-04
HOLT-4						1.196	0.966	94	67	96		- 3	6.46E-0€	6.352+05	>1.00E-04
RPMI-6226	0.735 0.486	-				0.444	0.318	Źε	92	54	- 0 -	- 25	1.188-06	7.195-06	>1.00E-04
SR Non-Small Cell Lu			c. , , o	0.01	••••										00= 04
A549/ATCC	0.377	1.362				0.942	0.579	104	9 3 9 3	101	57 52	21 23			>1.00E-04 >1.00E-04
EKVX						0.680	0.523	102	80 53	e 5	55	21			>1.00E-04
HOF-62						1.013	1.142	3.6	6.6	92	51	7€	>1.00E-C4		
HOP-92 NCI-H226	0.607		0.914			0.671	0.524		104	102		-14			>1.00E-04
NCI-H23					1.063	0.664	0.634	94	96	e 5	57 74	27			>1.00E-04 >1.00E-04
NCI-H322M	0.624	1.629				1.366	0.799	105	98 101	وِهِ 104	45	15			>1.00E-04
NCI-H460						0.609	0.319 0.360	105	103	102	•	-13			>1.00E-04
NCI-H522	0.413	0.954	1.000	0.969	0.965	0.361	0.300	100							
Colon Cancer COLO 205	0.326	1.242	1.250	1.163	1.006	0.450	0.285	101	94	74		-23			>1.00E-04
HCC-2998	0.590	1.321	1.301	1.316		0.944	0.514	97	100	104	46 42	-13 17			>1.00E-04 >1.00E-04
HCT-116	0.161					0.616	0.341 0.626	105 90	9-3	161	45	22			>1.00E-04
HCT-15	0.317	1.751	1.602 0.640			0.960	0.020	97	96	101	61	8	1.632-05	>1.01E-04	>1.00E-04
HT29	0.166 0.294	0.€59 1.232			1.227	0.672	0.484	101	96	ة ق	40	20	6.662-06	>1.CCE-04	>1.00E-04
KM12 SW-620						0.652	0.466	100	93	92	56	36	2.24E-05	>1.C1E-C4	>1.00E-04
CNS Cancer							0.547	101	9.6	86	52	46	2.07E-05	>1.01E-04	>1.00E-04
SF-26E	0.463	1.301	1.309	1.262	1.166	0.696	0.647	93	79	74	22	ō	2 PAF-06	>1 CIE-04	>1.00E-04
SF-295	0.400 0.367	1.077	1.029 0.802		0.619	0.393	0.176	63	90	67	1	-55	2.66E-06	1.05E-05	£.29E-05
SF-539 SNB-19	0.571		1.464	1.461	1.490	1.013	0.769	101	103	104	50	23		>1.0:0E-04	>1.00E+04 >1.00E+04
SNB-75	0.361	0.628		0.633	0.510		0.420	وة	102 96	52 97	-11 30	16	1.06E-06		>1.00E-04
U251	0.199	0.851	0.868	0.625	0.629	0.396	0.255	103	90	51	30	-			
Helanoma	0.303	1.076	0.996	0.997	0.945	0.593	0.416	91	91	6.5	45	25	7.64E-06	>1.00E-04	>1.00E-04
LOX IMVI MALME-3M	0.151	0.952	0.949	0.934		0.691		55	96	64	46	27	£.09E-06	>1.00E-04	(>1.00E-04
K1.4	0.196	0.527	0.496	0.521	0.522	0.337	0.214	90	3.6	96 93	43	5 12	7.35E-06	>1.00E-04	>1.00E-04 >1.00E-04
SK-MEL-2	0.746	1.404	1.408				0.624	101 106	96 90	76	46	43	E. 77E-06	>1.00E-0	4 >1.00E-04
SK-MEL-2E	0.576		1.313	1.201 1.123	1.106	0.913	0.319	110	107	72	36	26	4.31E-06	>1.00E-0	< >1.00E-04
SK-MEL-5 UACC-257	0.034	1.051	1.159	1.155		0.919		105	105	74	65	8.8	>1.00E-04	>1.00E-0	4 >1.00E-04
UACC-62	0.577				1.633	0.959	0.796	104	96	67	31	16	4.65E-06	3	4 >1.00E-04
Ovarian Cancer						1 262	1 022	94	95	94	6£	4.2	4.761-05	>1.00E-0	4 >1.00E+04
IGR-OV1	0.515		1.666	1.697	1.663	1.362		103	وَوَ	67	31	13	4.57E-06	>1.00E-0	4 >1.00E-04
OVCAR-3	0.293		1.120	1.016	1.043	0.967		106	90	94	€ 5	5 c	>1.00E-04	>1.CCE-C	4 >1.00E-04
OVCAR-5	0.393		0.893	0.882	0.667	0.662		107	104		62	26 29	2.128-05	>	4 >1.00E-04 4 >1.00E-04
OVCAR-6	0.267		0.932	0.937	0.911	0.743		9E 104	0 0	95 96	70 43	10	7.56E-06	>1.00E+C	4 >1.00E-04
sk-ov-3	0.466	0.975	0.994	0.923	0.965	0.666	0.519	104	-0	2 0	•				
Renal Cancer 786-0	0.200	0.913	1.003	0.888	0.844	0.543	0.436	113	96		46	3.3	9.01E-06	>1.0E-0	4 >1.00E-04
A496	1.081				1.569	1.331		104	96		51	20	1.112-03)	4 >1.00E+04 4 >1.00E+04
YCHI	0.406	1.396	1.401	1.430	1.436	1.206		100 95	103 72		61 36	5.2 3.2	3 777-06	>1.00E-0	4 >1.00E-04
CAKI-1	0.466				0.792	0.636		95			52	42	1.44E-0	>1.CGE-0	4 >1.00E-04
RXF-393	0.704 0.371				1.201	0.936		91	93		63	40	3.67E-0	>1.00E-0	4 >1.00E-04
SN12C TK-10	0.371			1.207	1.122	1.167	0.977	92			91	59	>1.00E-0	>1.EGE-0	4 >1.00E-04 4 >1.00E-04
DO-31	0.593	1.442	.1.440	1.370	1.431	1.228	1.030	100	92	95	75	52			
Prostate Cancer				- 000	1 042	0.636	0.395	104	٥٥	93	42	12	7.002-0	6 >1.0E-0	4 >1.00E-04
PC-3 DU-145	0.302	1.096	1.130	1.086	1.012			100				- 1	3.75E-0	6 E.SCE+0	5 >1.00E-04
Breast Cancer	0.333				1.010								c : 25 0	: :CE=0	04 >1.00E-04
MCF7	0.423	1.174 و	1.207	1.176				104			36 61	46 23	1 067-0	5 33 CCF+0	D4 >1.00E-04
MCF7/ADR-RES		0.90	0.91	0.697				102				22	2 7 5 5 - 0	5 >3 CCE-6	D4 >1.00E-04
MDA-ME-231//								103		2 67	51	€ 3	>1.00E-0	4 >1.10E-	C4 >1.00£-04
HS 576T '		4 1.319 0 0.961						101	. 69			-66	6.222+0	7 4,29E-	06 4.05E-05 06 4.94E-06
MDA-ND-433	0.21		0.670	0.651	0.275	0.04		£ 5				-60 36	2.E0E-0	6 >" 10E+	04 >1.00E-04
BT-549	0.47	6 0.62	2 0.90	0.649				123				77	>1.00E-0	4 >1.30E-	04 >1.00E-04
T-47D	0.71	1 2.00	2 1.984	4 1.999	1.622	1.47	0 1.709								





: D- 673163 -1/0-1/3	Experiment ID: 9409SC89	Test Type: 8	Units: Molar
rt Date: October 27, 1994	Test Date: September 26, 1994	QNS:	MC:
n: octahydrophomopsin a	Stain Reagent: Dual-Pass	SSPL: 0FLC	

						Log10	Concent	ration							
	Time				al Densi					ent Gr					
el/Cell Line	Zero	Ctrl	-6.0	-7.0	-6.0	-5.0	-4.0	-6.0 -	-7.0 -	-6.0 -	-5.0	-4.0	GI 50	ICI	1C50
kemia							0 242	90	96	6.2	6	- 3	2.71E-06	5 325-05	>1.00E-04
CCRF-CEM	0.250	0.846	0.785	0.823	0.736	0.301	0.242	106	95	88	~25	-49	2.16E-06	5 995-06	>1.00E-04
HL-60 (TB)	0.213	0.710	0.741	0.686	0.649	0.160 0.261	0.109	100	106	92	22	14			>1.00E-04
K-562	0.129	0.726	0.727	0.774		0.261	0.454	103		105	39	20			>1.00E-04
MOLT-4	0.281	1.162	1.167	1.266	1.202	0.239	0.131	110	96	84	7	-33			>1.00E-04
RPMI-8226	0.196	0.784	0.841	0.776	0.692 1.456	0.600	0.432	94	96	92	27	15			>1.00E-04
SR		1.562	1.403	1.509	1.436	0.000	0.432	24	2.0	72			1.102 00	.1.002 04	>1.00E-04
-Small Cell Lun		1.402	1.450	1.442	1.370	0.849	0.507	105	104	97	47	14	8.66E-06	>1.00E-04	>1.00E-04
A549/ATCC EKVX	0.688	1.701	1.649	1.673	1.583	1.317	1.133	95	97	8.6	62	44			>1.00E-04
HOP-62	0.834	1.736		1.704	1.779	1.486	1.222	103	9€	105	72	43	5.72E-05	>1.00E-04	>1.00E-04
NCI-H226	0.591	0.929	0.879	0.843	0.876	0.702	0.461	8.5	75	8.5	33	-22	4.68E-06	3.97E-05	>1.00E-04
NCI-H23	0.455	1.575	1.684	1.778	1.623	1.229	0.593	110	116	104	69	12	2.17E-05	>1.00E-04	>1.00E-04
NCI-H322M	0.556	1.391	1.394	1.383	1.313	0.969	0.775	100	õõ	91	49	26	9.70E-06	>1.00E-04	>1.00E-04
NCI -H460	0.219	1.062	1.058	1.051	1.028	0.462	0.239	99	ōē	96	29	2			>1.00E-04
NCI-H522	0.434	1.065	1.059	1.059	0.992	0.435	0.468	99	ōč	88	-	5	8.40E-06	>1.00E-04	>1.00E-04
on Cancer															
COLO 205	0.208	0.975	0.956	0.972	0.745	0.216	0.037	97	100	70	1	-82	1.95E-06		4.11E-05
NCC-2996	0.262	0.873	1.115	1.211	1.084	0.687	0.221		•	135	•	-16	1.33E-05		>1.00E-04
HCT-116	0.230	1.417	1.467	1.447	1.413	0.721	0.392	104	103	100	41	14			>1.00E-04
HCT-15	0.717	2.847	2.756	2.780	2.787	1.946	1.060	96	97	97	58	1€			>1.00E-04
HT29	0.148	0.817	0.772	0.755	0.749	0.351	0.191	93	5.7	90	30	6			>1.00E-04
KM1.2	0.907	1.983	2.068	2.236	2.404	1.586	0.833	108	124	139	63	-6			>1.00E-04
SH-620	0.140	0.690	0.664	0.678	0.618	0.325	0.319	95	36	87	34	32	4.92E-06	>1.00E-04	>1.00E-04
Cancer							. :		• • •	86	43	22	(305 06		>1.00E-04
SF-268	0.367	1.294	1.305	1.290	1.161	0.764	0.572	101	100	72	-27	-65			4.04E-05
SF-295	0.554	1.239	1.154	1.158	1.046	0.405	0.194	88	8 E 9 S	95	27	-32			>1.00E-04
SF-539	0.517		1.496	1.437	1.440	0.780	0.353	101 100	95	99	59	38			>1.00E-04
SNB-19	0.587	1.709	1.704	1.675	1.696	1.254	1.014	90	111	89	-7	27	2.55E-06	71.00L-04	>1.00E-04
SNB-75	0.367	0.801	0.757	0.850	0.753	0.342	0.483 0.185	96	200	90	20	-3		7 30F-05	>1.00E-04
0 251	0.191	0.874	0.848	0.869	0.806	0.327	0.165	50		,,	10		3	11302 03	71.002 01
anoma	0 370	1.142	1.113	1.138	1.069	0.724	0.617	97	100	92	52	39	1.33E-05	>1.00E-04	>1.00E-04
TOX IHAI	0.279	0.509	0.510	0.431	0.493	0.724	0.122	101	70	94	24	-51			9.70E-05
M14	0.563	1.347	1.436	1.420	1.391	0.858	1.033	111	106	106	38	60			>1.00E-04
SK-MEL-2 SK-MEL-28	0.305	0.940	0.972	0.901	0.743	0.489	0.564	105	54	69	29	41	2.96E-06	>1.00E-04	>1.00E-04
SK-MEL-20	0.354	1.478	1.402	1.533	0.864	0.388	0.287	93	105	4.5	3	-19	6.35E-07	1.37E-05	>1.00E-04
TDACC-257	0.709	1.939	1.910	1.898	1.755	1.149	1.159	96	97	8.5	36	37	5.14E-06	>1.00E-04	>1.00E-04
rian Cancer	05	1.555													
IGROV1	0.346	1.494	1.567	1.579	1.480	0.947	0.733	108	107	99	52	34			>1.00E-04
OVCAR-5	0.377	0.957	0.968	0.921	0.933	0.710	0.518	102	94	96	57	24			>1.00E-04
OVCAR-8	0.550	2.624	2.741	2.595	2.626	1.832	1.160	106	5 ق	100	62	29			>1.00E-04
SK-0V-3	0.423	0.862	0.796	0.851	0.770	0.543	0.377	€5	9€	79	27	-11	3.63E-06	5.21E-05	>1.00E-04
ial Cancer											0.5			.1 005 0	
786-0	0.434	1.623	1.873	1.963	2.204	1.748	1.181	104	110	127	95	54			>1.00E-04
A498	0.561	0.917	0.933	0.917	0.926	0.734	0.617	104	100	103	49	16			>1.00E-04
ACHN	0.306			1.138	1.048	0.830	0.495	90 90	96	86 92	61 63	22 26			>1.00E-04 >1.00E-04
SN12C	0.636			1.625		1.283	0.924		ē€	101	87	51			>1.00E-04
TK-10	0.399	1.068	1.047	1.042	1.073	0.980	0.739	97	2.6	101	67	31	>1.00E-04	>1.00E-0.	71.002-04
ostațe Cancer							7 447	ро	100	90	37	21	5 76F-06	>1 DOE-0	4 >1.00E-04
PC 3	0.063		3 063	3.359		1.852	0.440	165	106	95	19				5 01.00E-14
DO-145	0.459	1.560	1.610	1.654	1.500	0.776	0.440	100	100		*.	•			
est Cancer	0 350		1 200	1 262	1.261	0.576	0.498	115	106	108	34	26	€.13E-06	>1.00E-0	4 >1.00E-04
MCF7	0.259			1.253	1.261	1.536		117	100	200	66	7.6			3 UÜE-UÇ
MCE // Auh = hz.o MDA =MB = 231 / ATO	C.634	1 6+0	1 4 KG			1.166		100		Î E 5	5.5	7.0	1.23E 05	91,00E C	4 91.00E-04
HS 578T	0.586					0.655		90		72	13	-10	2.37E-06		5 >1.00E-04
HDA-HB-435	0.283					0.405		100		59	13	-14	1.58E-06	3.05E-0	5 >1.00E-04
MDA-N ·	0.263						0.255	101	9.5	51	- 9	- 23	1.02E-06	7.09E-0	€ >1.00E-04
BT-549	0.606							111	75	€7	57	37			4 >1.00E-04
T-47D	0.775		2.071					95	122	89	45	48	7.81E-06	>1.00E-0	4 >1.00E-04
- ··-						,									

Dose Response Curves

Report Date: October 21, 1994

I BI Date. September 20. 19.7

MO_MID Delte Range	HIS 578T MDA-MB-435 MDA-N BT-549 T-47D	Breil Cancer MCF7 MCF7/ADR-RES MCF/ADR-RES	Prosinte Cancer PC-3 DU-145	786-0 A498 AGIN SN12C TK-10	IOROVI OVCAR-8 OVCAR-8 SK-OV-3 SK-OV-3	MEINODIA MIA MI4 SK-MEL-28 SK-MEL-28 SK-MEL-28 UACC-337	CNS Concer SP-268 SP-295 SP-399 SP-399 SNB-19 SNB-15 U251	Colon Cancer Colon (205 HCC-2998 HCT-116 HCT-15 HT29 KM12 KM12 SW-620	ASASMATICC EKVX HOP-62 NCI-H226 NCI-H231 NCI-H321 NCI-H321 NCI-H322 NCI-H322	Leukemia CCRP-CEM HL-60(TB) K-622 MOLT-4 RPMI-8226 SR	Panel/Cell Line
-5.13 0.95 2.0%	-5.980 -5.980 -5.980 -5.11	-5.21 -4.80 -4.91	-5.24 -5.32	> 4.00 -4.50 -4.63 > 4.63	74.0 7.7.7 7.7.7 7.7.7	.4.88 -5.37 -5.53 -6.08 -5.29	-5.17 -5.78 -5.34 -4.56 -5.59 -5.43	5.71 4.88 5.15 4.82 5.33 4.82 5.31	-5.06 -4.24 -4.24 -5.01 -5.01 -5.02 -5.08	5.57 5.67 5.40 5.17 5.13	1.0810 0150
	<u>-</u> †µ	<u>بلی</u>			_I lia	*	11-1			गन्ग	G150
-4.20 1.07 1.27	4.52 4.52 5.15 > 4.00	V 4.00	> .4.00 .4.12	V V 1.00	V 4.00 V 4.00 V 4.00	> 4.00 > 4.00 > 4.00 > 4.00 > 4.00	> 4.00 5.27 4.54 > 4.00	.4.99 .4.21 > .4.00 > .4.00 > .4.00 > .4.00	V V V V V V V V V V V V V V V V V V V	.4.27 .5.22 > .4.00 > .4.00 > .4.00	Log ₁₀ TGI
		V	V	> 4 30 > 4 30 > 4 30 > 4 30	V 1 2 3 4 5 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	V V L L L L L L L L L L L L L L L L L L	1		1	14.76 14.76 14.76	-

Experiment ID: 9502RM1c Test Type: 8 Units: Molar

eport Date: March 28, 1995 Test Date: February 13 1 QNS: SHP MC:

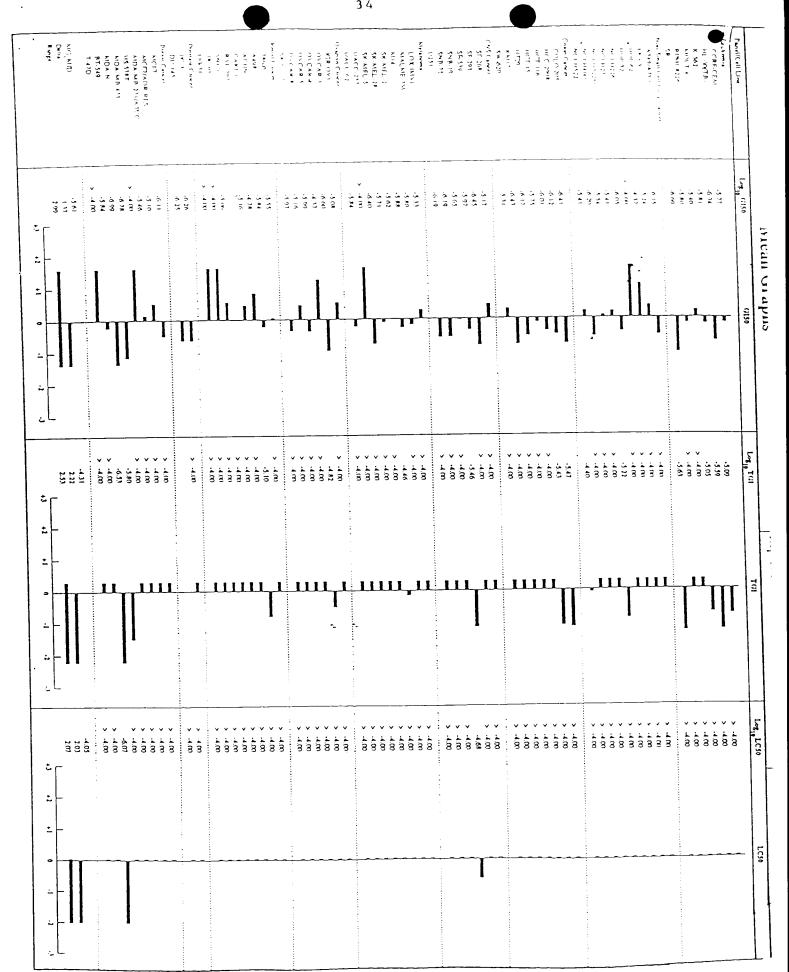
OMI: Phomopsinamine A Stain Reagent: Dual-Pass SSPL: 0FLC

						1 10	Concent						
	Time		Mean	Optical	l Densi		concerna		Exits:	-1 3:	5 - 7. 1.		
Panel/Cell Line	lero	Ctrl				-5.0	- : . 0	- t C -		5 . S	1.6		GI 50 TGI 1050
Leukemia										_	- 7,	- 2 4	1.69E-06 6.09E-06 >1.00E-04
CCRF-CEM		1.761				0.591	0.416	101	٠.	1.		- 4.5	4.56E-07 2.60E-06 >1.00E-04
HL-60 (TE)		1.622	1.679			0.371 0.369	0.312	100	16:	4.3		-36	1.56E-06 6.92E-06 -1.00E-04
K-562	0.382		1.370			0.961	0.793	104		£	25	ې	4.02E-06 >1.00E-04 >1.00E-04
MOLT-4 RPHI-8226	0.735			1.580		0.790	0.769	1 C 7	٠.	€ 1	E	4	1.60E-06 >1.00E-04 >1.00E-04
RPM1-6220 SR	0.486				0.53€	0.412	0.366	10:		ج	-15	- 1 .	2.04E-07 2.37E-06 +1.00E-04
Non-Small Cell Lu		t											7.06E-07 >1.00E-04 >1.00E-04
A549/ATCC	0.377	1.339				0.577	0.447	č.	1.	4 4 - <u>c</u>	11	3.6	5.E1E-06 >1.00E-04 >1.00E-04
EKVX	0.402					0.659 0.659	0.629	د د	11.	3 6	÷.	4.5	2.70E-05 >1.00E-04 >1.00E-04
HOP-62	0.391					1.110	0.970	128	I : :		Çξ	3 9	>1.00E-04 >1.00E-04 >1.00E-04
HOP-92	0.761					0.525	0.446	114	114	4.7	-14	- 17	8.95E-07 5.99E-06 >1.00E+04
NCI-H226	0.607 0.419					0.669	0.674	101	č t	- 3	3.3	3.4	3.85E-06 >1.00E-04 >1.00E-04
NCI = H23 NCI = H322M	0.624		1.602			0.644	0.785	104	111	7.3	2.5	2.7	2.90E-06 >1.00E-04 >1.00E-04
NCI-H460		1.263	1.266	1.267		0.316	0.329	100	101	37	12	- 4	6.35E-07 >1.00E-04 >1.00E-04
NCI-H522	0.413	1.073	1.071	1.084	0.691	0.642	0.316	100	1:1	7.2	35	-24	3.932-06 3.94E-05 >1.00E-04
Colon Cancer					• •••	0.246	0.179	3.9	£ :	2.6	-24	- 45	3.91E-07 3.40E-06 >1.00E-04
COLO 205			1.317	1.156 1.284		0.402	0.396		103	43		-33	7.55E-07 3.73E-06 >1.00E-04
HCC-2996	0.590 0.161	1.266	1.219	1.229		0.343	0.256	93	63	5 C	16	٤	9.87E-07 >1.00E-04 >1.00E-04
HCT-116 HCT-15	0.317	1.667	1.21-				0.393		5 }	řē	22	6	1.76E-06 >1.00E-04 >1.00E-04
HT29	0.166	0.631	0.620		0.429	0.193	0.190	è٤	101	4.0		4	6.76E-07 >1.00E-04 >1.00E-04
1041.2	0.294	1.445	1.397			0.397	0.301	96	£ :	2 €	٥	1	3.70E-07 >1.00E-04 >1.00E-04
SW-620	0.156	0.691	0.869	0.637	0.660	0.453	0.364	97	ē 3	71	40	∃ 7	4.89E-06 >1.00E-04 >1.00E-04
CNS Cancer					1.079	0.920	0.755	9.6	çı	÷4	47	3.0	6.77E-06 >1.00E-04 >1.00E-04
SF-268		1.431	1.410		0.554	0.400	0.400	103		24		- c	3.53E-07 >1.00E-04 >1.00E-04
SF-295	0.400	1.038	1.055 0.669		0.640	0.213	0.153	102	c ı	<u>5</u> 3	-45	- € O	1.06E-06 3.46E-06 2.09E-05
SF-539 SNB-19	0.571	1.365	1.372		1.063	0.617	0.742	9 6	è١	€1	3 C	2.2	2.22E-06 >1.00E-04 >1.00E-04
SNB-75	0.381	0.626	0.664	0.650	0.470	0.406	0.430	116	11:	3-€	10	20	6.51E-07 >1.00E-04 >1.00E-04
U251	0.199	0.893	0.920	0.615	0.481	0.273	0.279	104	€ 5	4.2	11	12	6.39E-07 >1.00E-04 >1.00E-04
Melanoma							0.357		ę :	7.5	37	2.2	4.66E-06 >1.00E-04 >1.00E-04
LOX INVI		0.982	:	0.942	0.765	0.467	0.610	100		5.5	26	25	1.57E-06 >1.00E-04 >1.00E-04
MALME-3M		1.037 C.569	1.035	0.552	0.407	0.201		99	ę :	5€	1	- 2	1.31E-06 3.48E-05 >1.00E-04
M14 SK-MEL-2	0.196		1.364		1.161	0.853	0.646	စ္င	9 1	⊃ €	17	16	2.40E-06 >1.00E-04 >1.00E-04
SK-MEL-26		1.166		1.102	0.944	0.725	0.853		€÷	€0	24	45	1.94E-06 >1.00E-04 >1.00E-04
SK-MEL-5	0.034		1.005	0.702		0.296		9.0	€÷	3 (27	- 9 - 3	4.00E-07 >1.00E-04 >1.00E-04 >1.00E-04 >1.00E-04 >1.00E-04
UACC-257	0.536				1.091	1.021		203 97	ē 1	 5 3	64 35	37	1.43E-06 >1.00E-04 >1.00E-04
TACC-62	0.577	1.662	1.621	1.770	1.255	1.029	1.047	2 /				- '	11432 00 721100 11
Ovarian Cancer	0.515	1.689	1.633	1.631	1.445	1.071	0.864	<u>ç 5</u>	5 :	ء	47	3.0	E.26E-06 >1.00E-04 >1.00E-04
IGR-OVI OVCAR-3	0.313				0.353	0.301	0.276	101		1.0	2	- €	2.54E-07 1.53E-05 >1.00E-04
OVCAR-4	0.467			1.189	1.095	0.662	0.767	ē £	101	ē S	٠,٠	4.5	4.29E-05 >1.00E-04 >1.00E-04
OVCAR-5	0.393			0.914	0.641	0.514		ة ة	111	5.0	2.5	3.5	1.02E-06 >1.00E-04 >1.00E-04 6.65E-06 >1.00E-04 >1.00E-04
OVCAR-6	0.267	1.196		1.211	1.126	0.658		100	151	5 2 5 1	4.2	2.2	1.06E-06 >1.00E-04 >1.00E-04
SK-OV-3	0.466	1.011	1.012	0.997	0.747	0.470	0.490	100	7		· ·	•	
Renal Cancer	0.200	0.949	1.006	0.955	0.716	0.396	0.350	301	11.	ۍ	26	2.0	2.79E-06 >1.00E-04 >1.00E-04
786-0	1.061		1.006	1.470	1.283	1.007		• • •		€1	-7	-1€	1 45F-06 7.91E-06 >1.00E-04
A496 ACHN	0.406		1.476		1.157	0.970	0.603	102	101	71	5.3	3 €	1.66E-05 >1.00E-04 >1.00E-04
CAKI-1	0.466				0.630	0.685		6 6		7.5	45	4.6	6.95E-06 >1.00E-04 >1.00E-04 >1.00E-04 >1.00E-04
RXF-393	0.704	1.582		1.447	1.195	0.602		6.6		56	11 46	5 O 3 O	6.61E-06 >1.00E-04 >1.00E-04
SN12C	0.371		1.201	1.236	1.133	0.633		6.6	91 101	111	7.3	7.3	>1.00E-04 >1.00E-04 >1.00E-04
TK-10	0.62		•:	1.090	1.142	0.967		1 C 2		1	5 3	5.3	>1.00E-04 >1.00E-04 >1.00E-04
00-31	0.593	1.476	1.492	1.513	1.452	1.066	1.000	101					
Prostate Cancer PC-3	0 30.	2 1 164	1 153	1.039	0.627	0.473	0.392	102	£ 5	36	2.0	2.0	5.54E-07 >1.00E-04 >1.00E-04
PC-3 DU-145	0.30	1.029	1.031	0.964	0.563			100		3.5	-12	1	5.60E-07 - >1.00E-04
Breast Cancer	2.55	٠										_	7.82E-07 >1.00E-04 >1.00E-04
MCF7		3. 1.139						103		43 E5	27 46	9 21	6.02E-06 >1.00E-04 >1.00E-04 6.02E-06 >1.00E-04 >1.00E-04
MCF7/ADR-RES		0 2.037						9 6				- 1	3.452-06 >1.00E-04 >1.00E-04
MDA-MB-231/A								102		70			>1.00E-04 >1.00E-04 >1.00E-04
HS 578T		4 1.396 0 1.268		0.910				102		2.0		- 27	1.65E-07 1.59E-06 >1.00E-04
MDA-MB-435 MDA-N	0.32					0.02			51	- 5 B	- é 6		1 G3F-07 2.95E-07 E.46E-07
BT-549	0.47						2 0.617	110				43	1.43E-06 >1.00E-04 >1.00E-04
T-47D	0.71					1.46	4 1.643	ō.	3 10:	77	5 4	ع -	>1.00E-04 >1.00E-04 >1.00E-04

Dose Response Curves

Report Date: March 28, 1995

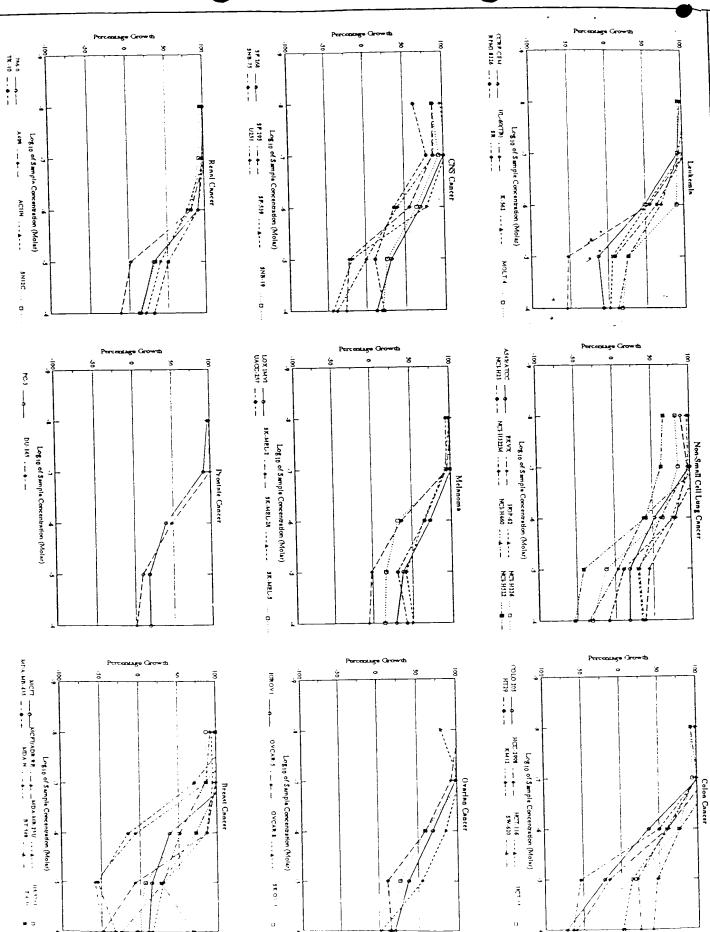
Test Date: February 13, 1995



National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results

C: L _73165 -K / 0-1 / 5	Experiment ID: 9409SC89	Test Type: 8	Units: Molar
port Date: October 27, 1994	Test Date: September 26, 1994	QNS:	MC:
MI: PHOMOPSINAMINE A	Stain Reagent: Dual-Pass	SSPL: 0FLC	

						Locin	Concent	ration					
	Time		Mean	Optica	al Densi				Ferce				
inel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-6.0	-7.0 -	-6.0 -	5.0 -	-4.0	GI50 TGI LC50
±ukemia											• •	-7	9.50E-07 6.21E-06 >1.00E-04
CCRF-CEM	0.250	0.793	0.779	0.757		0.216	0.232	97 104	93 363	49 56	-13 -53	-55	1.13E-06 3.28E-06 9.47E-06
HL-60 (TB)	0.213	0.691	0.710	0.706	0.481	0.101	0.096	104	100	53	- 55	2	1.14E-06 >1.00E-04 >1.00E-04
K-562	0.129	0.762	0.795	0.764	0.463	0.165	0.141	95	23	91	26	17	4.27E-06 >1.00E-04 >1.00E-04
MOLT-4	0.281	1.366	1.312	1.293	1.268	0.255	0.258	106	103	65	9	• •	1.86E-06
RPMI-8226	0.196	0.676	0.919 1.741	0.899	1.256	0.614	0.414	104	95	71	26	12	2.92E-06 >1.00E-04 >1.00F-04
SR	0.238		1./41	1.612	1.230	0.014	0.414	•••			• •		
on-Small Cell Lun	o ance	1.610	1.591	1.608	1.016	0.596	0.584	99	200	53	19	18	1.19E-06 >1.00E-04 >1.00E-04
A\$49/ATCC ERVX	0.688	1.691	1.579	1.652	1.493	1.128	1.074	€ 9	9.6	60	44	3.8	6.79E-06 >1.00E-04 >1.00E-04
HOP -62	0.834	1.662	1.701	1.666	1.457	1.074	1.115	105	101	75	29	34	3.51E-06 >1.00E-04 >1.00E-04
NCI-H226	0.591	1.104	1.010	1.024	0.913	0.521	0.409	82	64	63	-12	-31	1.48E-06 6.95E-06 >1.00E-04
NCI-H23	0.455	1.521	1.625	1.647	1.288	0.571	0.413	110	112	78	11	-9	2.62E-06 3.48E-05 >1.00E-04
NC1-H322M	0.556	1.478	1.444	1.454	1.114	0.842	0.867	96	67	61	31	36	2.27E-06 >1.00E-04 >1.00E-04
NCI -H4 60	0.219	1.146	1.184	1.252	0.563	0.252	0.142	104	111	37	4	-35	6.72E-07 1.23E-05 >1.00E-04
NCI-H522	0.434	1.347	1.035	1.000	0.803	0.254	0.201	66	62	40	-42	-54	3.58E-07 3.11E-06 4.88E-05
olon Cancer								3.00	103	36	-22	-72	6.17E-07 4.19E-06 3.65E-05
∞LO 205	0.208	1.003	1.074	1.023	0.495	0.163	0.059 0.107	109 109	113	60	-16	-59	1.37E-06 6.23E-06 6.16E-05
HCC-2998	0.262	0.891	0.947	0.974	0.642	0.221	0.107	99	713	63	14	1	1.82E-06 >1.00E-04 >1.00E-04
HCT-116	0.230	1.465	1.453	1.458	2.337	1.121	0.760	93	94	76	19	2	2.83E-06 >1.00E-04 >1.00E-04
ACT-15	0.717	2.858 0.793	0.801	0.803	0.470	0.069	0.054	101	102	50	-53	-64	9.97E-07 3.04E-06 9.27E-06
HT29	0.148	2.189	2.312	2.489	1.895	1.506	1.4.8	110	123	77	47	40	7.81E-06 >1.00E-04 >1.00E-04
RM12	0.140		0.778	0.831	0.549	0.283	0.306	93	100	59	21	24	1.75E-06 >1.00E-04 >1.00E-04
574-620	0.140	0.626	0.770	0.031	0.545	0.100							
NS Cancer SF-268	0.367	1.284	1.294	1.284	1.008	0.659	0.484	101	100	70	32	13	3.33E-06 >1.00E-04 >1.00E-04
SF-295	0.554	1.381	1.270	1.263	1.016	0.431	0.405	67	86	56	-22	-27	1.19E-06
SF-539	0.517	1.568	1.540	1.592	1.331	0.423	0.291	97	102	77	-18	-44	1.94E-06 6.45E-06 >1.00E-04
SNB-19	0.587	1.633	1.488	1.571	1.265	0.866	0.800	86	94	€5	27	20	2.44E-06 >1.00E-04 >1.00E-04
SNB-75	0.367	0.901	0.701	0.763	0.560	0.428	0.463	€3	7€	36	11	22	4.66E-07 >1.00E-04 >1.00E-04
0251	0.191	0.834	0.753	0.753	0.451	0.193	0.117	€7	€7	40	О	-39	6.25E-07 1.02E-05 >1.00E-04
iel anoma												5.6	4.55E-06 >1.00E-04 >1.00E-04
LOX IMVI	0.279	1.064	1.050	1.071	0.852	0.576	0,503	3.0	101	73	38	26 -6	5.96E-07 9.18E-06 >1.00E-04
SK-MEL-2	0.563		1.516	1.462	0.905	0.555	0.530	102 100	96 93	37 65	-1 42	49	4.37E-06 >1.00E-04 >1.00E-04
SK-MEL-28	0.305	0.975	0.974	0.929	0.740	0.584	0.636	100	50	32	17	14	5.39E-07 >1.00E-04 >1.00E-04
SK-MEL-5	0.354		1.704	1.671	0.778 1.564	0.574	1.252	95	95	66	31	42	2.85E-06 >1.00E-04 >1.00E-04
TACC-257	0.709	2.006	1.941	1.943	1.364	1.111	1.202			•••			
Warian Cancer	0.346	1.479	1.482	1.460	1.125	0.769	0.565	100	9.6	69	37	19	3.96E-06 >1.00E-04 >1.00E-04
IGROVI	0.346		0.881	0.834	C. 671	0.432	0.451	102	93	60	11	15	1.58E-06 >1.00E-04 >1.00E-04
OVCAR-5 OVCAR-8	0.550	-	1.238	1.426		1.016		81	103	€5	55	2	1.22E-05 >1.00E-04 >1.00E-04
SK-OV-3	0.423		0.908	0.935	0.705	0.551		101	107	59	27	14	1.88E-06 >1.00E-04 >1.00E-04
Senal Cancer	0.423												
786-0	0.434	2.015	2.010		1.875		0.664	100	98	91	31	15	4.87E-06 >1.00E-04 >1.00E-04
A496	0.561	0.980	1.024	0.985	0.906	0.570		111	101	8.2	2	-11	2.54E-06 1.47E-05 >1.00E-04
ACHN	0.306	1.259	1.245	1.263	1.041	0.692		50	100	77	41	21	5.50E-06 >1.00E-04 >1.00E-04 4.52E-06 >1.00E-04 >1.00E-04
SN12C	0.636		1.632	1.603	1.483	0.981		9€	93	82	33	13	1.05E-05 >1.00E-04 >1.00E-04
TK-10	0.399	0.995	0.984	0.998	0.944	0.700	0.585	9.6	100	91	50	31	1.032-03 21.002-04 21.002 04
Prostate Cancer						1 467	1.413	97	90	40	16	18	6.36E-07 >1.00E-04 >1.00E-04
PC-3	0.952					1.405		و و	99	4.6	10	10	8.97E-07 >1.00E-04 >1.00E-04
DO-145	0.459	1.595	1.581	1.567	0.999	0.572	0.467	27	2.2	40	10	*	
Breast Cancer	0.000		1.285	1.306	0.600	0.390	0.347	114	116	38	15	10	7.02E-07 >1.00E-04 >1.00E-04
MCF7	0.259			1.297		0.481		103	99	67	-7	-48	2.49E-06 8.44E-06 >1.00E-04
MCF7/ADR-RES				. 1.559		0.902		95	3 6	86	29	15	4.32E-06 >1.00E-04 >1.00E-04
MDA-MB-231/ATC	0.586			1.067		0.623		87	έ7	50	6	-5	1.02E-06 3.67E-05 >1.00E-04
MDA-MB-435	0.283					0.128		12€	71	-15	-55	-32	1.75E-07 6.66E-07
MDA-N	0.332		1 348			0.139		93		-€	-56	-49	2.49E-07 8.61E-07
BT-549	0.606					0.692				51	29	-25	1.14E-06 3.47E-05 >1.00E-04
1-47D	0.775				1.601	1.072	1.547	55	105	72	26	6.8	. >1.00E-04 >1.00E-04



36

	MQ_MID Delta Range	HS 5787 HD A-MB 435 MD A-N BT 549 T 47D	Bread Cancer MCF7 MCF7/ADR-RES MCF7/ADR-RES MDA-MB-231/ATCC	Provisite Cancer PC-3 DU-145	ACHN SN12C TK-10	Renal Cancer 786-0 A498	OVCAR-S OVCAR-8 SK-OV-3	Overlan Concer IGROVI	SK-MEL-28 SK-MEL-3	Melanoma LOX IMVI · SK-MEL-2	SNB-19 SNB-75 U251	CNS Cancer SF-268 SF-295 SF-539	HT29 KMI2 SW-620	HCC-2998 HCT-116 HCT-15	NCI-H460 NCI-H522 Colon Cancer	NCI-H226 NCI-H23 NCI-H322M	AS49/ATCC EKVX HOP-62	RPMI-R226 SR Non-Small Cell Lung Cancer	HL60(TB) K-562 K-0174	Panel/Cell Line Leukemia COR pia CEM	
Light Column Co	Γ	.5.99 .6.76 .5.60 .5.94	-6.15 -5.60 -5.36	6.20 6.05	3.10 3.34 4.98	.5.31 .5.60	4.91 -3.73	-5,40 -4 80	5.36 6.27 5.55	-5.34 -6.22	-5.61 -6.33 -6.20	-5.48 -5.92 -5.71	5.00 5.11 -5.76	5.74	-5.17 -5.45	5.54 5.58	5.92 5.17 7	5.73 5.53	-5,95 -5,94 -5,37	6.02	ı
161 15p L290 400 400 400 400 400 400 400	·	•11	1.	1	h	L		_1	1	T	ΤŢ*	الوجياً ا	1		1 1		Л ,		L.	T	GIS0
101 18,6 LC30 3(2) 4(3) 4(3) 4(4	÷	:	> 4.00 5.07 4.00	> 4.00 > 4.00	> 4.00 > 4.00	v 4.83	> 4.00 > 4.00	× × × × × × × × × × × × × × × × × × ×	\$ 8 8 £ 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	, v. 3.00 3.00 8.00	;		> 4.00 > 4.00	> 4.00 > 4.00	3.51 3.53	* 4.46 * 4.00	> 4.09 5.16	× 4.8		.5.21	Log _{io} TGI
\$F	÷		<u>-</u> T	11	11	H			11	Մ		T				1			11	Π	TGI
	=		8888	884	84.4	2 v v v 3 8 8 .	. v v	888	y 400	~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	× × 4 33	0 0 0 0 4 4 4 4 8 8 8 8	2 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	V V V V V V V V V V V V V V V V V V V		V V V A A A A A A A A A A A A A A A A A	 	. A 6	 4 k S	4(8) 5)(2	1.4810 LCS0

Example 2

The following data show the effect of phomopsin A on several human cancer cell lines growing *in vivo* in hollow fibres inserted subcutaneously and intraperitoneally in athymic mice, as employed by NCI to assess the *in vivo* anticancer potential of compounds (Hollingshead *et al.*, 1995). Significant cell growth inhibition and cytocidal activity in demonstrated.

Report printed on 07-MAY-97

EXPT NOT HESSI-0-HE SEX: F	E.ALUATI N DATE: 15-DEC-95 S ROLVING: 1	HOST. SOURCE	HOST: Athymic Nudes SOURCE: APA	ς.		IMPLANT DATE: C8-DEC-95 SIAGING DATE: 11-DEC-95	TE: C	8-DEC-95 1-DEC-95
					%T/C			
	TREATMENT		LOX IMVI	· 	COLO 205		OVCAP-3	-3
Grp NSC Bo. Dose	Dose/Units Rt 37/4/50	No. of No. of Mice Fibers	1.	SC	1.0	35	d	SC
D-673162	ୁତ · 4, ଠିବ,	в В	>100 >1	>100	63	49	35	on to
58 D-673162 20.00	20.00 mg/kg/dose IP QP + 4, Pa; 3	3	. 37 ' >1	>100	5.8	85	36.	>100

	n) Inj. Vol.:0.1 ml/10gm body wt n) Inj. Vol.:0.1 ml/10gm body wt
	15%) (Unknown) 15%) (Unknown)
	in Saline + Tween 90 (0.05%) (Unknown) in Saline + Tween 80 (0.05%) (Unknown)
	£.3.
	(Dese= (Dese=
	6731627 6731627
VEHICLES	Grp 57 -> NSC # Grp 58 -> NSC #

COMMENTS for HF591-0-HF

Report printed on 07-MAY-97

EXPT NO: HF590-0-HF SEX: F	HF	EVALUATION DATE: 15-DEC-95 SOURČE/PINE: 1	HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	Nudes		IMPLAN	IMPLANT DATE: 07-DEC-95 STAGING DATE: 11-DEC-95	07-DEC-95 11-DEC-95
	FNGWERGOF	· ·		-		D/IR		}	
	TUTUT	1,171		NCI-H23	.н23	MDA-MB-231	3-231	Š.	24-850
Grp NSC	nose/Units Rt	Schedule	No. of No. of Mice Fibers	IP	SC	IP	SC	118	SC
57 D-673162	o se	QD X 4, Day 4	8	81	96	. 46	72	>100	2017
58 D-673162	20.00 mg/kg/dose IP QD X 4, Day 4	QD X 4, Day 4	3	>100	>100	44	46	>100	>100

VEHICLES

673162/ 1 (Dose- 30.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162/ 1 (Dose- 20.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt NSC # Grp 57 -> Grp 58 ->

COMMENTS for HF590-0-HF

Report printed on 01-APR-96

EXPI NO: HES90-0-HE SEX: F	<u>.</u>	FOR LUATION DATE: 15-DEC-95 SOURCE/LINE: 1		HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	Nudes		IMPLAN	IMPLANT DATE: 07-DEC-95 STAGING DATE: 11-DEC-95	07-DEC-99
		4					%T/C (Net Growth)	Growth)		
17.	TREATMENT		1		NCI-H23	.н23	MDA-MB-231	B-231	MS	SW-620
orp NSC No. No. Dose/Units	# l	Schedule	No. of No. of Mice Fibers	No. of Fibers	IP	SC	IP	SC	IP	SC
52 D-673162 30.00 mg/kg/dose IP QD : 4, Day 4	IP QD 4I	4, Day 4	£	е	16	94	30	63	>100	>100
58 D-673162 20.00 mg/kg/dose IP QC · 4, Da. 4	1P QC	4, Da, 4	3	E.	>100	>100	28	29	>100	>100

VEHICLES

inj. vol.:0.1 ml/10gm body wt	inj. Vol.:0.l ml/l0gm body wt
(Unknown)	(Unknown)
Tween 80 (0.05%)	Tween 80 (0.05%) (Unknown)
00) : in Saline +	(1) In Saline +
1 (Dose- H.	1 (Dose= '
673162/	673162/
NSC #	NSC .
3rp 57 ->	irp 58 ->

COMMENTS for HF590-0-HF

Report printed on 01-APR-96

EXPT NO: HF591-0-HF SEX F	EVALUATION DATE: 15-DEC-95 SOURCE/LINE: 1	HOST: Ath) SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	ndes		IMPLAN	IMPLANT DATE: 08-DEC-95 STAGING DATE: 11-DEC-95	08-DEC-95
	•				%T/C (Net Growth)	Growth)		
1	TREATMENT	ı	LOX IMVI	1/1	COLO 205	205	OVCAR-3	R-3
Grp NSC No. Dose/Units	Rt Schedule	No. of No. of Mice Fibers	1 P	SC	IP	SC	IP	SC
57 D-673162 30.00 mg/kg/dose	30.00 mg/kg/dose IP QD X 4, Day 3	3	>100	>100	59	34	-18	22
58 D-673162 20.00 mg/kg/dose	20.00 mg/kg/dose IP QD X 4, Day 3	3 3	29	>100	48	81	-15	>100

	Inj. Vol.:0.1 ml/10gm body wt Inj. Vol.:0.1 ml/10gm body wt	
	(Unknown) (Unknown)	
	Grp 57 -> NSC # 673162/ 1 (Dose- 30.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt Grp 58 -> NSC # 673162/ 1 (Dose- 20.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt	
	1 (Dose-	
	673162/ 673162/	
	NSC #	
VEHICLES	Grp 57 -> NSC # Grp 58 -> NSC #	

COMMENTS for HTS91-0-HT

Report printed on 07-MAY-97

Grp NSC NSC Dose/Units Rt Schedule No. of	EXPT NO: HF581-0-HF SEX: F	-HF	EVA CATION DATE: 17-NOV-95	HOST: Athyr SOURCE: AFA	HOST: Athymic Nudes SOURCE: AFA		IMPLAN	IMPLANT DATE: 13-NOV-95	36VON-8
Dose/Units Rt Schedule No. of No. of Mise Fibers IP SC IP SC 62 30.30 mg/kg dose IP 2D + i, Da, 4 3 2 85 96 100 92 62 20.30 mg/kg dose IP 2D + i, Da, 4 3 3 3 3 3 90			REATVENT		NCI - 115.22	* UACC-	6.5	1,25.	
D-673162 30.30 mg/kg dose IP 2D + 1, Da, 4 D-673162 20.30 mg/kg dose IP 2D + 1, Da, 4 3 3 7	Grp NSC No. No.	Dose/Units		No. of No. of Mise Fibers		a I	SC	<u>6.</u>	SC
2-673162 2C.30 mg/kg dose IP 3D · 1, Da, 4 3 3 70 >100 97 90	0-673162	30, 34, mg/km, duse	में हिंदी हैं के महिल्ला है	. m m		100	92	>100	a) n
	8 0-673162	20.30 mg/kg dose	IP 2D · 1, Da, 4	3 3		ţ.6	06	06	от О

	# 673162' (Dose- '.3:) in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162' ; (Dose3C) . In Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt
	in Saline + Tween 80 (0.05%) (Unk in Saline + Tween 80 (0.05%) (Unk
	673162/ (Dose- 1.00) 673162/ (Dose- 1.00)
VEHICLES	Grp 7 -> NSC #

COMMENTS for HF581-0-HF

Report printed on 01-APR-96

	EVALUATION DATE: 17-NOV-95 SOURCE/LINE: 1	HOST. SOURC	HOST: Athymic Nudes SOURCE: APA	Nudes		IMPLAN STAGIN	IMPLANT DATE: STAGING DATE: 13-NOV-95	3-NON-81
TNOMERGOR	t Nu				%I/C (Net Growth)	Growth)		
HIVENI	1117	; ;	NCI-H522	H522	UACC-62	-62	U251	51
Dose/Units Rt	Schedule	Mice Fibers	IP	SC	IP	SC	119	SC
di esop/f	30.00 mg/kg/dose IP QD X 4, Day 4	3 2 3 3	59	91	100	8 1	>100	9.1
dI asop/5	20.00 mg/kg/dose IP QD X 4, Day 4	3 2 3 3	18	>100	95	61	83	96

VEHICLES

Inj. Vol.:0.1 ml/l0gm body ⊮t	Inj. Vol.:0.1 ml/10gm body wt
(Unknown)	(Unknown)
Tween 80 (0.05%) (Unknow	iline + Tween 80 (0.05%) (Unknown)
1 (Dose- 30.00) : in Saline + Tw	: in Sa
(Dose- 30.	1 (Dose- 20.00)
673162/	673162/
NSC	NSC •
Grp 7 ->	Grp 8 ->

COMMENTS for HF581-0-HF

Report printed on 07-MAY-97

EXPT NO: HE582-0-HF SEX: F		CALCATION DATE: 17-NOV-95 C.RCE/TINE: 1	HOST	HOST: Athymic Nudes SOURCE: APA	ndes		IMPLAN	IMPLANT DATE: STAGING DATE: 13-NO7-95	3-X0X-6
	TREA "MEN!			, , , , , , , , , , , , , , , , , , ,	-435	81/C	-5	SE	SE-295
Grp NSC No. No.	Dose/Units Rt	Schedule	No. of No. of Mice Fibers	IP	SC	IP	SC	15	30
. 2-673162	30,00 mg/k1/dose 12 QD * 4. Daz 4	. Sav 4	3 2 3	7.1	69	(1) (1)	26	о 10	6
3 0-673162	20.00 mg/kg/dose IP QD + 4, D4+ 4	£ - FC -	m	81	8.7	5°. 80	9.2	>100	5014

673162/ 1 (Dose- 1).[0] : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162/ 1 (Dose- 1).[0] : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt Grp 7 -> NSC # VEHICLES

COMMENTS for HF582-0-HF

Report printed on 01-APR-96

EXPT NO: HF582-0-HF SEX: F	-HF	EVALUATION DATE:) SOURCE/LINE:	DATE: 17-NOV-95		HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	udes		IMPLAN STAGIN	IMPLANT DATE: STAGING DATE: 13-NOV-95	13-NOV-95
								%T/C (Net Growth)	Growth)		
	1	TREATMENT				MDA-MB-435	-435	OVCAR-5	R-5	SF	SF-295
Grp NSC No. No.	Dose/Units	Rt Schedule	• 11	No. of No. of Mice Fibers	No. of Fibers	IP	SC	IP	SC	IP	SC
7 D-673162.	30.00 mg/kg/dose	30.00 mg/kg/dose IP QD X 4, Day 4		mм	3 2	62	58	38	06	89	>100
8 D-673162	20.00 mg/kg/dose	20.00 mg/kg/dose IP QD X 4, Day 4		æ	æ	74	8.2	87	94	>100	>100

673162/ 1 (Dose- 30.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162/ 1 (Dose- 20.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt NSC . Grp 7 -> Grp 8 -> VEHICLES

COMMINIS for HF582-0-HF

Report printed on 01-APR-96

EXPT NO: HF580-0-HF SEX: F	۲. ۲.	EVALUATION I	ION DATE: 09-NOV-95		HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	Nudes		IMPLAN STAGIN	IMPLANT DATE: STAGING DATE: 05-NOV-95	05-NOV-95
		TREATMENT						%I/G (Net Growth)	Growth)		
				; 	:	LOX IMVI	IMVI	COLC	COLO 205	OVCAR-3	4R-3
No. No.	Dose/Units	Rt	Schedule	Mice	Mice Fibers	IP	SC	IP	SC	IP	SC
D-673162	45.00 mg/kg/dose IP QC × 4, Fay 2	IP QC × 4, Da	۰۶ 2	9	1	86	080	>100	64	61	>100
8 D-673162	30.00 mg/kg/dose IP QD x 4, Day 2	IP QC x 4, Da	19. 2	3	е	88	85	58	98	25	37

VEHICLES

Inj. Vol.:0.1 ml/10gm body wt	Inj. Vol.:0.1 ml/10gm body wt
5%) (Unknown)	(Unknown)
line + Tween 80 (0.05%) (Unknown	Tween 80 (0.05%)
: in Sa	: in Saline + '
45.00	30.00
1 (Dose= 45.00)	l (Dose- 30
673162/	673162/
NSC #	NSC •
Grp 7 ->	Grp 8 ->

COMMENTS for HF580-0-HF

Report printed on 01-APR-96

EXPT NO: HF579-0-HF SEX: F	EVALUATION DATE: 09-NOV-95 SOURCE/LINE: 1	HOS1	HOST: Athymic Nudes SOURCE: APA	. Nudes		IMPLANT	IMPLANT DATE: 02-NOV-95 STAGING DATE: 05-NOV-95)2-NOV-95)5-NOV-95
					\$T/C (Ne	%I/C (Net Growth)		
	TREATMENT		NCI	NCI-H23	MDA-	MDA-MB-231	SW-620	520
Grp NSC Dose/Units	Rt Schedule	No. of No. of Mice Fibers	뫕	SC	IP	SC	IP	SC
 	45.00 mg/kg/dose IP QD X 4, Day 3	3 2	4	-41	>100	>100	78	78
8 D-673162 30.00 mg/kg/dose	30.00 mg/kg/dose IP QD X 4, Day 3	3	09	21	66	>100	16	9.6

VEHICLES

Inj. Vol.:0.1 ml/10gm body wt Inj. Vol.:0.1 ml/10gm body wt	
(Unknown) (Unknown)	
Tween 80 (0.05%) (Unknown Tween 80 (0.05%) (Unknown	
e= 45.00) : in Saline + Tv e= 30.00) : in Saline + Tv	
45.00)	
1 (Dose= 1 (Dose=	
673162/ 673162/	
NSC I	
Grp 7 -> Grp 8 ->	

COMMENTS for HF579-0-HF

Report printed on 07-MAY-97

EXPT NO: HF580-0-HF SEX: F	ALUÁCION DATE: 09-NOV-95 ; URĜE/ČINE: 1	HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	udes		IMPLAN STAGIN	IMPLANT DATE: STAGING DATE: 05-NOV-45	36-AON-60
					D/I%	D	•	
	TREATMEN	1	LOX IMVI	IMVI	302 000	205	OVCAR-3	R-3
Grp NSC NC. No.	Dose/Units Rt Schedule	No. of No. cf Mice Fibers	IP	SC	IP	SC	dī	SS
2-673162	45.00 mg/kg/dose 11 Cl ' 4. Liy 2	3 1	86	84	>100	72	62	>700
8 D-673162	30.00 mg/kg/dose IF QL > 4, Pay 2	3	06	88	67	8 9	9	66

VEHICLES

1 (Dcse= '5,30) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 1 (Dcse= 0.30) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162/ 673162/ NSC + Grp 7 -> Grp 8 ->

COMMENTS for HF580-0-HF

Report printed on 07-MAY-97

Grp NSC No. Dose/Units Rt Schedule 7 D-673162 45.00 mg/kg/dose IP QD X 4, Day 3	EVALUATION DATE: 09-NOV-95 SOURCE/LINE: 1	HOST: Athy SOURCE: APA	HOST: Athymic Nudes SOURCE: APA	MI TS	IMPLANT DATE: 02-NOV-95 STAGING DATE: 05-NOV-95
TREATMENT Dose/Units Rt 62 45.00 mg/kg/dose IP QD X 4, Day 3				\$T/C	
Dose/Units Rt S.00 mg/kg/dose IP QD X 4, Day 3	TREATMENT		NCI-H23	MDA-MB-231	SW-620
62 45.00 mg/kg/dose IP QD X 4, Day 3	±.	No. of No. of Mice. Fibers	IP SC	IP SC	IP SC
	1 1		88	>100 >100	82 83
	mg/kg/dose IP QD X 4, Day 3	,			0
8 D-673162 30.00 mg/kg/dose IP QD X 4, Day 3	mg/kg/dose IP QD X 4, Day 3	3	77	99 >100	60 86

673162/ 1 (Dose- 45.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt 673162/ 1 (Dose- 30.00) : in Saline + Tween 80 (0.05%) (Unknown) Inj. Vol.:0.1 ml/10gm body wt NSC # Grp 7 -> Grp 8 -> VEHICLES

COMMENTS for HF579-0-HF

Finally, it is to be understood that various alterations, modifications and/or additions may be introduced into the composition and/or arrangement of steps previously described without departing from the spirit or ambit of the invention.

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DATED: 29 September, 1999

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10 INDUSTRIAL RESEARCH ORGANISATION

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